The frequency and nature of adverse events in acute Irish hospitals: the Irish National Adverse Events Study

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Doctor of Medicine

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Professor Anne Hickey

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Candidate Thesis Declaration

I declare that this thesis, which I submit to RCSI for examination in consideration of the award of a higher degree Doctor of Medicine is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research programme this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own. I have not already obtained a degree in RCSI or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and acknowledged within the text.

Signed;

Student Number: 13126377

Date: 2 March 2016
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<th>Description</th>
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<tbody>
<tr>
<td>AE</td>
<td>Adverse event</td>
</tr>
<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research &amp; Quality</td>
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<tr>
<td>AIDS</td>
<td>Acquired Immunodeficiency Syndrome</td>
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<tr>
<td>BMJ</td>
<td>British Medical Journal</td>
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<tr>
<td>CAES</td>
<td>Canadian Adverse Events Study</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CINAHL</td>
<td>Cumulative Index to Nursing and Allied Health Literature</td>
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<tr>
<td>CIS</td>
<td>Clinical Indemnity Scheme</td>
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<tr>
<td>CT</td>
<td>Computerised Tomography</td>
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<tr>
<td>D</td>
<td>Detected</td>
</tr>
<tr>
<td>DALY</td>
<td>Disability Adjusted Life Year(s)</td>
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<td>DRG</td>
<td>Diagnosis Related Group(s)</td>
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<tr>
<td>Embase</td>
<td>Excerpta Medica database</td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>GTT</td>
<td>Global Trigger Tool</td>
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<tr>
<td>HIQA</td>
<td>Health Information and Quality Authority</td>
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<td>HMPS</td>
<td>Harvard Medical Practice Study</td>
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<tr>
<td>HSE</td>
<td>Health Service Executive</td>
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<tr>
<td>ICD-10AM</td>
<td>International Classification of Diseases, 10th revision, Australian Modification</td>
</tr>
<tr>
<td>ICD-10AM/ACHI/ACS</td>
<td>International Classification of Diseases, 10th revision, Australian Modification/ Australian Classification Health Interventions/ Australian Coding Standards</td>
</tr>
<tr>
<td>ID</td>
<td>Identifier</td>
</tr>
<tr>
<td>IHI</td>
<td>Institute for Healthcare Improvement</td>
</tr>
<tr>
<td>INAES</td>
<td>Irish National Adverse Events Study</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute of Medicine</td>
</tr>
<tr>
<td>IQR</td>
<td>Inter-quartile Range</td>
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<tr>
<td>MCC</td>
<td>Major Clinical Category</td>
</tr>
<tr>
<td>MEDLARS</td>
<td>Medical Literature Analysis and Retrieval System</td>
</tr>
<tr>
<td>MEDLINE</td>
<td>MEDLARS Online</td>
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<tr>
<td>MeSH</td>
<td>Medical Subject Headings</td>
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<td>MRN</td>
<td>Medical Record Number</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>NCC MERP</td>
<td>National Coordinating Council for Medication Error Reporting and Prevention</td>
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<tr>
<td>NIMS</td>
<td>National Incident Management System</td>
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<tr>
<td>NAEMS</td>
<td>National Adverse Events Management System</td>
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<td>NHS</td>
<td>National Health Service</td>
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<td>PsycINFO</td>
<td>Psychological abstracts database</td>
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<tr>
<td>O</td>
<td>Occurred</td>
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<tr>
<td>OR</td>
<td>Odds Ratio</td>
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<tr>
<td>QAHCS</td>
<td>Quality in Australian Health Care Study</td>
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<tr>
<td>RCPI</td>
<td>Royal College of Physicians of Ireland</td>
</tr>
<tr>
<td>RCSI</td>
<td>Royal College of Surgeons in Ireland</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SRE</td>
<td>Serious Reportable Event(s)</td>
</tr>
<tr>
<td>STROBE</td>
<td>Strengthening the Reporting of Observational Studies in Epidemiology</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Presentation

Summary

Irish healthcare has undergone extensive change with spending cuts and a focus on quality initiatives. However, little is known about adverse event occurrence. This thesis assesses the frequency and nature of adverse events in Irish hospitals and compares the results to international adverse events data, using a systematic review methodology and conducting the Irish National Adverse Events Study (INAES).

Retrospective patient chart review based on the Harvard Medical Practice Study methodology was undertaken. A random sample of adult in-patient admissions from 2009 was selected from eight hospitals, stratified by region and size, across the Republic of Ireland. 1,574 patient charts (53% female, mean age 54 years) underwent two-stage review (stage-one: nurse review for triggers; stage-two physician review of triggered charts for adverse events) with electronic data capture. Results were weighted to reflect the national case mix. The impact on adverse event rate of differing application of international adverse event criteria was also examined.

In stage-one 45% of charts were triggered. The prevalence rate (risk) of adverse events in admissions was 12.2% (95% CI 9.5% – 15.5%), with an incidence of 10.3 events per 100 admissions (95% CI 7.5 – 13.1). Over 70% of events were considered preventable. Two-thirds were rated as having a mild to moderate impact on the patient, 10% resulted in permanent impairment and 6.7% contributed to death. A mean of 6.1 added bed days was attributed to events, representing an additional expenditure of €5,550 per event.

This first study of adverse events in Ireland reported similar rates to other countries. In a time of austerity, adverse events in adult in-patients were estimated to cost approximately €200 million. These results provide important baseline data on the adverse event burden and, alongside web-based chart review, provide an incentive and methodology to monitor future patient safety initiatives.
Acknowledgements

This research was funded by the Health Research Board of Ireland within the Research Collaborative in Quality and Patient Safety (RCQPS/2013/1). Funding for the adaptation of the web-based chart review tool was provided by the Office for Nursing and Nursing Midwifery Services Director, Health Services Executive.

I gratefully acknowledge the support and assistance provided by the eight participating hospital sites and especially their medical records and HIPE departments for providing access to the patient charts reviewed for the study. I am extremely grateful for the hard work and collegiality of the nurse and physician reviewers. I acknowledge the national HIPE and cost data provided by the Healthcare Pricing Office.

I would like to thank the INAES Working Group (Professor David Williams, Professor Anne Hickey, Professor Ronan Conroy, Dr Sarah Condell, Dr David Vaughan, Dr Paul O’Connor, Ms Gillian Walsh) for their assistance throughout the study and valued input as co-authors on study publications. I would like to thank Fiona Hickey for her work on the systematic review.

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1 CHAPTER 1: Introduction

*It may seem a strange principle to enunciate as the very first requirement in a Hospital that it should do the sick no harm.*

Florence Nightingale, Notes on Hospitals, Third edition 1863, London

The ability of medicine (and healthcare) to cause harm is not new. Doctors have long been aware of the possibility through the Hippocratic Oath (the English version of the original includes the words “I will willingly refrain from doing injury”) and the well-known phrase also attributed to Hippocrates “primum non nocere” (“first do no harm”). However, it was in 1999 with the publication by the Institute of Medicine (IOM) in the United States of the report *To Err is Human: Building a Safer Healthcare System* that the possibility of being harmed in hospital comprehensively caught the attention of the general public, clinicians and healthcare managers.(1)

1.1 The concept of patient safety

The *To Err is Human* report used data from the Harvard Medical Practice Study (HMPS) to estimate that one million Americans were being injured in hospitals annually, with between 44,000 and 98,000 deaths.(1, 2) The report stated that more people die each year due to harm in hospitals than from breast cancer, traffic accidents, or acquired immunodeficiency syndrome (AIDS).(1) Widespread media attention resulted. The report highlighted the impact of adverse events and emphasised the need to measure and reduce their occurrence in all areas of healthcare.(1) A call for a national effort on patient safety was made with the objective of reducing the rate of medical error by half within five years.(3)
The United Kingdom (UK) Department of Health published *An Organisation with Memory* a year later. In this the Department estimated that hospital adverse events occur in approximately 10% of admissions, amounting to over 850,000 patients annually in the National Health Service (NHS) alone. Like *To Err is Human*, it recommended building a safer health system by developing a national focus on patient safety, learning from failures and changing from a blame culture to one of safety.

These reports provided the impetus for the development of patient safety initiatives and organisations across the world. The United States Congress, in response to *To Err is Human*, set aside US$50 million a year for patient safety research and the Agency for Healthcare Research and Quality (AHRQ) was nominated as the lead federal agency for patient safety. Other American organisations grew their role in patient safety such as the Institute for Healthcare Improvement (IHI), the National Patient Safety Forum and the Joint Commission on Accreditation of Healthcare Organizations. In the UK the government set up the National Patient Safety Organisation within the NHS. A 2002 World Health Assembly Resolution to coordinate, facilitate and accelerate patient safety improvements around the world resulted in the World Health Organization (WHO) establishing a Patient Safety Programme and launching the WHO World Alliance for Patient Safety in 2004.

Prior to the *To Err is Human* report, hospitals collected risk data for managing litigation claims and occupational health and safety; there was a low awareness of patient safety. After the report, the conversation of clinicians and healthcare managers changed from “Is there a problem?” to “What can we do about it?” The patient safety agenda was being framed. WHO defined patient safety as “the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum”. There was a large increase in number of patient safety publications and their focus moved from an emphasis on malpractice to the safety culture within the organisation.
The concept of a system, rather than an individual, at fault became accepted into the mainstream of healthcare management. (3)

1.2 Defining adverse events in healthcare

1.2.1 WHO patient safety taxonomy

One of the first initiatives of the WHO Patient Safety Programme was to commence work on a taxonomy. (7, 9) It was acknowledged that the patient safety field was being hampered by lack of consistency in terminology, making research synthesis difficult. (10) Two surveys of the literature published in 2006 found 17 and 24 definitions of error and 14 of adverse event. (9) This led to the development and publication of a conceptual framework for the International Classification for Patient Safety in 2009. (7, 9) The definitions below are taken from this framework.

Healthcare-associated harm is defined as “harm arising from or associated with plans or actions taken during the provision of healthcare, rather than an underlying disease or injury”. (9) The delivery of healthcare occurs within a complex environment of multiple decision makers, heterogeneous patients, diagnostic and prognostic uncertainty, a large knowledge base and an evolving range of new and complex treatments. Harm to a patient can occur at any time in the healthcare process. Harm involves “impairment of structure or function of the body and/or any deleterious effect arising there from” and “includes disease, injury, suffering, disability and death.” (9)

A patient safety incident is defined as “an event or circumstance which could have resulted, or did result, in unnecessary harm to a patient”. A near miss is “an incident which did not reach the patient”, i.e. the patient experienced no harm. An adverse event (or harmful incident) is defined as “an incident that resulted in harm to a patient”. The investigation of adverse events and near
misses may highlight errors. Errors are defined as “failure to carry out a planned action as intended or the application of an incorrect plan”.(9)

Some adverse events and near misses are considered preventable. Preventable is defined by WHO as “being accepted by the community as avoidable in the particular set of circumstances”.(9) Not all adverse events will be considered preventable and this judgement can change with advances in healthcare quality.(11)

1.2.2 Harvard Medical Practice Study adverse event definition
The Harvard Medical Practice Study (HMPS) analysed data from 1984, prior to the WHO taxonomy. It defined an adverse event as “an injury that was caused by medical management (rather than the underlying disease) and that prolonged hospitalization, produced a disability at the time of discharge, or both”.(2) This study reviewed over 30,000 patient charts in New York hospitals to determine the rate of adverse events for which there were the quantifiable outcomes of death, disability at discharge and prolonged stay. The definition that was used in the Harvard Medical Practice Study is a subset of the WHO definition which includes all incidents of harm. As it was initially commissioned to assess the potential for no-fault compensation in New York State, the Harvard study further analysed events to establish what proportion of these were negligent (i.e. due to substandard care).

The major legacy of the Harvard Medical Practice Study has been to highlight the issue of patient harm and to stimulate similar large scale studies.(12) Its methods have been used as the foundation for adverse event studies in the United States of America, Australia, New Zealand, the UK, Spain, the Netherlands, Africa, Latin America, Brazil, Portugal and Canada.(13-31) In order to be consistent with other international adverse event studies, the Irish National Adverse Events Study (INAES), which forms
the major part of this thesis, is based on the Harvard Medical Practice Study methodology and adverse event definition.

1.3 The frequency and nature of adverse events

1.3.1 Large hospital-based adverse event studies
The majority of information on national rates of adverse events comes from large reviews of patients’ hospital charts using a two-stage trigger tool methodology developed in the Harvard Medical Practice Study. In stage one of the method, reviewers examine the patient’s hospital chart\(^1\) for presence of any potential adverse events which are present on a list of clinical scenarios, called “triggers” (e.g. healthcare-associated infection, adverse drug reaction, unexpected death). Charts that have one or more triggers are then reviewed in stage two and the existence of an adverse event determined. These international chart review studies have demonstrated that between 3% and 17% of admissions are associated with an adverse event and a substantial proportion of these (one- to two-thirds) are preventable (Figure 1.1).(2, 14, 16, 18, 23, 27, 28, 30-34)

\(^1\) The term chart is used to describe the documentation file or record for a patient’s hospital encounters. It includes documentation by healthcare professionals during admissions, emergency department and out-patient visits, investigation results, medications and fluids prescribed, and summaries of surgical and non-surgical procedures.
A 2008 systematic review by de Vries and colleagues of eight of these large patient chart review studies (including national studies from New Zealand and Canada, state-wide studies in New York, Utah/Colorado, and South Australia/New South Wales, and large hospital studies in Boston and England) found a median overall incidence of adverse events of 9.2%, with over half of events being operation-related (40%) or drug-related (15%). The majority of the adverse events resulted in little or no disability, but an important minority (a median of 14%) caused permanent disability (7%) or death (7%).(35) Most of the events occurred in the hospital (median 81%), with the operating theatre and the patient’s own room being the most frequent locations; a further 15% occurred outside of hospital (mainly in the physician’s office) and in 5% the location was unknown.(35)
Many studies have found a higher risk for patients being cared for under surgical specialties compared with medical specialties, (14, 35-40) although some did not find a statistically significant difference. (14, 21, 41). In the de Vries systematic review a median of 58% of adverse events occurred in patients cared for by a surgical service compared with 24% under medical services. (35). However the distributions of surgical and medical admissions in the populations were not given so that the proportion of admissions associated with adverse events (i.e. rate of adverse events) in the specialty groups could not be calculated. When this was performed in the Australian study the rate of adverse events in surgical admissions (which constituted 38% of the sample) was higher than in all admissions (21.9% versus 16.6%). (30, 36). However the study in Utah/Colorado found no difference in adverse event rates between the specialties; nonetheless the greatest proportion of adverse events were surgical. (41)

The majority of events which occurred in surgical specialties were directly related to the operation. (38, 41, 42) In Gawande’s analysis of surgical adverse events from the Utah/Colorado study, three categories accounted for half of all surgical events – technique-related complications (24.2%), wound infections (11.2%), and postoperative bleeding (10.8%). (41) Surgical adverse events have been associated with a lower proportion of deaths (42, 43) and preventable adverse events than events occurring under the medical services. (13, 42, 43)

Most adverse event studies have demonstrated an increased risk of adverse event occurrence in older patients. (2, 13-16, 27, 29-33) However, some did not find a difference with age and suggest this link may instead be with factors such as length of stay and co-morbidity. (21, 24, 44)
There is some evidence that particular categories of events (diagnostic and drug-related events) were more preventable than other categories. Drug-related adverse events were also more likely to occur outside the hospital and result in lower impact events than other types of events. Cardiovascular drugs (including anticoagulants), centrally acting drugs (in particular opiates), and antibiotics have been the most common categories implicated in adverse event studies.

A longer length of stay has been associated with a greater risk of an adverse event but this is difficult to interpret because adverse events themselves prolong the hospital stay. The longer mean length of stay for patients with adverse events was found to be in the order of six to ten additional days.

Adverse event studies have differed in their association between type of admission (emergency or elective) and risk of an adverse event. Where reported, most have found an increased risk of an adverse event with emergency (urgent) admission but in one study this was an increase in preventable events only. In two studies emergency admissions had no significant increase in risk or had a decreased adverse event risk.

A consistent relationship with hospital size has also not been found. The Canadian national study found higher adverse event rates in larger hospitals but the Spanish one found rates highest in small hospitals. The Dutch study conducted an additional analysis comparing adverse event rates between hospitals and departments. In their modelling they adjusted for patient (age, sex, co-morbidity, diagnosis) and hospital stay (emergency/elective, length of stay, surgical admission, hospital type, etc.) characteristics. They found more variation between hospital departments within a hospital (adverse event rate range 3.2% - 19.7%) than between
hospitals (range 4.2% - 15.6%). Differences between hospitals were mainly explained by hospital type rather than patient mix, whereas the differences between departments were due to both patient mix and department type. They concluded that there is more room for improvement on the department level than the hospital level and that patient safety initiatives should consider patient safety culture and outcomes within and between departments.(40)

1.3.2 Global burden of adverse events

Most of the large patient chart review studies were conducted in the developed world. The lack of data in developing and transitional countries and the possibility of higher adverse event rates due to greater risks from unsafe injections, blood products and reduced access to healthcare led the WHO Alliance for Patient Safety to facilitate patient chart review studies in Africa and Latin America.(6, 51) The eight African countries studied had adverse event rates of 2.5% - 18.4% and in the five Latin American countries studied the range was 7.7% - 13.1%.(13, 29)

Since its initiation, the WHO Patient Safety Programme has spent considerable effort reviewing the literature to quantify the burden of specific adverse events and determine global patient safety priorities. Their 2008 report summarising the evidence for patient safety globally provided the following information: healthcare-associated infections are estimated to affect around 5% - 10% of people admitted to hospital; falls represent two in five patient incidents of which 30% result in injury; and decubitus ulcers have a prevalence of 10% - 15%.(51)

In complementary work, the WHO studies in Africa and Latin America, alongside epidemiological data from the literature, were used to estimate the global burden of adverse events.(52) The incidence of seven adverse events (adverse drug events, catheter-related urinary tract infections, catheter-related bloodstream infections, healthcare-associated pneumonia, venous
thromboembolism, falls and decubitus ulcers) in hospitalised patients were put into a model which allowed the authors to estimate the global numbers of injuries and their impact in disability adjusted life years (DALYs). The authors concluded that there are 43 million injuries each year due to medical care and that nearly 23 million DALYs are lost as a consequence, with the burden highest in low and middle income countries.\(^{(52)}\) These figures rank adverse events (based only on the seven included types) as the 20\(^{th}\) highest cause of morbidity and mortality in the world.\(^{(52)}\)

### 1.3.3 Adverse events in out-of-hospital settings

Methods are being developed to estimate errors and adverse events in the community. For example, a Scottish study modified the Institute for Healthcare Improvement out-patient adverse event trigger tool for primary care and found 9\% of patient records contained an adverse event, with a frequency of 2\% per consultation.\(^{(53)}\) A New Zealand study further adapted the tool and estimated a rate of harm of 7 incidences per 100 consultations.\(^{(54)}\) Another study asking primary care physicians to fill out reporting forms identifying errors and adverse events after each clinical encounter, found that 5\% of consultations resulted in harm.\(^{(55)}\) Many of these adverse events occurring in primary care will impact on secondary care. Several of the hospital patient chart review studies have found that approximately 5\% of the adverse events detected in hospital originated in primary care.\(^{(14, 30, 33)}\) A review of patient records in nursing homes found that adverse drug events occurred at a rate of 10 per 100 resident months.\(^{(56)}\) A trigger tool for nursing homes has been developed by the Institute for Healthcare Improvement.\(^{(57)}\)
1.3.4 Adverse events in the Republic of Ireland

There is no systematically recorded data on the national prevalence or incidence of adverse events in the Republic of Ireland.

The Clinical Indemnity Scheme (CIS) is the scheme under which the State Claims Agency manages all clinical negligence claims taken against public healthcare organisations. It collects reports on adverse clinical incidents occurring within these organisations. This data is publically available only at an aggregated level. It includes near misses and is not broken down by hospital setting, making meaningful calculation of prevalence problematic. The only data about adverse events on the State Claims Agency website is a joint report with the Health Service Executive (HSE) published in 2012. (58) This report presents the overall number of adverse event reports (85,918) in 2011 broken down by event type in tables and graphs. The main incident categories were slips/trips/falls (32%); violence/harassment/aggression/abuse (11%); medication incidents (8%); treatment incidents (7%); and peri-natal incidents (7%). (58) The accompanying media release states that these events occurred in 4.5 million patient contacts. (59) This figure covers all public healthcare services in secondary care and the community so that without more information about where, or to whom, these events occurred, the incidence of adverse events for hospital patients cannot be calculated.

Breathnach and colleagues performed a review of over 42,000 clinical incidents which were reported to the CIS from Irish surgical specialties between 1 January 2004 and 31 May 2010. (60) They found that the majority (72%) of incidents occurred in general surgery and orthopaedics, and that slips, trips and falls were the most frequent incident category reported (32% of cases). The next most common categories were medication error and peri-operative incidents (percentages not given). (60) The most common outcome type was “no apparent injury/reaction” at 80%, and 1% of incidents was fatal. The authors also examined the 478 claims closed by the CIS over the same
period and found that the distribution of event type was different compared with the incident reporting data - half of the claims cases were peri-operative/procedure incidents, followed by treatment incidents, infection control incidents and diagnosis incidents, i.e. slips, trips and falls did not feature highly on the claims data. (60)

Irish adverse event data previously came from a survey of infections and medication error reports. A hospital survey in the Republic of Ireland, England, Wales and Northern Ireland estimated an overall prevalence of healthcare-associated infections of 7.6%, with the lowest prevalence in the Republic at 4.9%. (61) An analysis of over 6,000 internal hospital voluntary medication error reports in 2006/7 from eight hospitals or hospital networks in Ireland showed 95% result in no patient harm. (62) Medication error reports from a single Irish hospital between 2005-2009 also demonstrated that 5% were associated with harm and patient harm was most frequently associated with opiates (pain due to missed or insufficient doses), insulin (hyper or hypoglycaemia) or cardiovascular medications (abnormal blood pressure and arrhythmias). (63) Two chart review studies of surgical mortality have been performed in Ireland but these did not report on the relationship of the deaths recorded with adverse events. (64, 65)

1.3.5 The human and financial costs of adverse events
The occurrence of an adverse event has a number of detrimental effects on both patients and healthcare workers including physical and/or psychological harm, a loss of trust in the healthcare system, and reduced staff morale. In addition to physical and psychological harm for patients, both patients and families report feelings of guilt and regret for not being able to circumvent the adverse event themselves. (66)
The impact of adverse events on healthcare workers is an important consideration; staff are often described as the “second victims” of adverse events. (67) When an event occurs in an organisation the identity of the healthcare professional involved is likely to be known. Colleagues may conclude the event was the result of incompetence because the evidence may demonstrate a misread investigation or a warning not heeded. (68) The person is likely to feel isolated and ashamed. They may suffer depression or turn to alcohol and drugs or overwork. (68) Errors are associated with poorer quality of life, lower empathy and burnout in the staff implicated. (69) There is rarely an outlet for review of the event and healing, even though clinicians have an ethical and professional responsibility to talk about error and disclose. (70) Error is common; half of junior doctors report making a medical error during training. (69) While most discuss these with other junior doctors, only half will discuss their mistakes with their seniors. (69, 71) One study showed that despite 90% of patient outcomes after error being serious, only a quarter of junior doctors talked to the patient or their families about the event. (71)

The economic costs of adverse events are substantial. Adverse events are associated with prolonged hospitalisation and on this basis alone are expensive, without consideration of additional societal costs such as reduced productivity and poorer population health. WHO estimates that 20% - 40% of all health spending is wasted due to poor quality care. This includes costs due to additional hospital stays, litigation, infections, disability, lost productivity, and medical expenses, amounting to US$19 billion per annum in the United States. (72)

In the UK, longer hospital stays due to adverse events were estimated to cost the UK government £2 billion per year, with preventable adverse events costing £1 billion. (4, 28) A Scottish adverse events study calculated that based on additional hospital days, adverse events cost Scotland £297 million per annum. (34) In Australia preventable adverse events were estimated to
account for 8% of hospital bed days and cost the Australian healthcare system AUD$4.7 billion a year.\(^{(30)}\)

A Dutch patient chart review study used their direct medical costs of excess length of stay and additional medical procedures to calculate the national cost impact of adverse events at €355 million. Preventable adverse events contributed to 3% of bed days and cost €161 million - equivalent to 1% of the health budget. The average cost for events occurring in surgical specialties was almost double that of medical (€6122 versus €3831).\(^{(73)}\)

A detailed analysis of the adverse events identified in the patient chart review study in Utah and Colorado, calculated the cost of each adverse event in terms of time off work, lost household productivity, disability and healthcare costs (including in-patient days, out-patient visits, physiotherapy and occupational therapy visits, home health visits, nursing home care, medication, and medical supplies).\(^{(74)}\) Healthcare costs made up half of the total adverse event costs; the largest contributors to healthcare costs were nursing home care (48%) and in-patient days (43%: non-intensive 31%, intensive 10% and in-patient physician 2%). Therefore more than half of healthcare costs were borne outside of the hospital.\(^{(74)}\) The authors estimated adverse events to contribute 4.8% of per capita health care expenditures in these states.\(^{(74)}\) The New Zealand patient chart review study used their own data on additional bed days plus information collected on additional procedures after an adverse event to calculate that adverse events would cost the medical system NZ$870 million, representing 30% of public hospital expenditure. When out-of-hospital costs were included, based on the Utah/Colorado study estimates, this figure doubled to over NZ$1.6 billion.\(^{(74, 75)}\)
Litigation is also a significant cost in many countries. In Ireland the State Claims Agency settled 1,939 clinical claims at a settlement cost of €95 million in 2014 and in 2015 has an outstanding liability of over €1billion. (76)

1.4 Human error theory and a systems approach

At approximately the same time as the 1999 IOM report *To Err is Human*, the *BMJ* published Reason’s seminal article on human error and the systems approach to error. (77) He described the prevailing dogma surrounding error as person-based, where an individual is at fault and redress involves punishment and modifying a person’s future behaviour. He then theorised that adverse events occur within a system and are consequences of “upstream” system factors in the workplace and organisational processes. An adverse event is not then the result of one person making a mistake at the frontline; rather conditions in the system enable the adverse event to occur. Therefore the defence against error should come from the system’s series of defences rather than targeting individual deviation. (77)

Reason depicted this in the Swiss cheese model (Figure 1.2) where he describes the layers of the cheese as representing defences within the system, each of which contain holes. Holes can arise because of latent conditions in the defence barriers or when an active failure (error) by a person occurs. Layers vary in their susceptibility to the development of latent conditions - less so if the defence layer is engineered for safety or process controlled, but more vulnerable if it is dependent on human behaviour. Usually an injury to the patient does not occur because propagation of the hazard is prevented by the next defence layer. However, when the holes in the slices of Swiss cheese align, the system’s defences have failed, the hazard propagates resulting in a loss, i.e. the error reaches the patient and an injury occurs. (77)
Figure 1.2 The Swiss cheese model of how defences, barriers, and safeguards may be penetrated by an accident trajectory.
Source: Reason, Human error: models and management. BMJ 2000;320:768-70

This is illustrated with the example of the defence layers in a hospital which act to prevent a patient with a known allergy to penicillin being given a penicillin-based medication:

Layer 1: Allergy recorded in hospital’s electronic patient administrative data
Layer 2: Allergy documented at admission in patient and medication charts
Layer 3: Pharmacist medication reconciliation on admission
Layer 4: Allergy alert placed on or near the patient (bracelet, bedside sign)
Layer 5: Pharmacist daily ward round reviews medication chart
Layer 6: Doctor checks for allergy prior to prescribing
Layer 7: Dispensing protocol checks for allergy
Layer 8: Nurse asks patient/checks for allergy prior to administering the medication
Future layers: computerised prescribing, automated dispensing systems (pharmacy robots dispense medication), barcode reconciliation (medication scanned against prescription and patient)

In this way, if a patient with an allergy does receive a penicillin-based medication it is not solely the “fault” of the nurse giving the medication or the doctor writing the prescription or the pharmacist dispensing the drug, rather the hazards or latent conditions in the defence layers of the system aligned to enable the active error(s) to reach the patient.

Thus in a systems approach, system failings rather than individuals are the subject of investigation.(77) A systems approach assumes humans are fallible and errors are inevitable.(4) Such an approach identifies the prevalence and nature of adverse events so that when errors are made, the apparent causes and underlying factors are reviewed to generate ideas for system improvements. Systems are therefore designed for safety, making it difficult for adverse events to occur whilst mitigating the ones that do happen. In this way errors are detected and corrected before harm is caused.(78) When errors are made, the proximal causes and underlying systems are reviewed to generate ideas for system redesign.(78)

Nevertheless, healthcare systems around the world have been slow to learn. An example is the continuing fatalities from intra-thecal vincristine despite multiple reports and investigations, enhanced drug labelling, protocols and equipment modifications.(79) There remain difficulties in identifying and managing latent failures in healthcare. In healthcare, adverse events occur within a complex socio-technical system. These systems are diverse and challenging to change. The aviation industry is often held as an exemplar of an industry that was able to change its culture and markedly improve safety. In aviation, confidential reporting of near-misses through the Aviation Safety Reporting System provides a rich source of data from which safety lessons
can be learned.(80) The aviation industry expects systems to go wrong and builds safety into its designs, whilst healthcare expects systems (and individuals) to perform correctly all the time. However, healthcare is a significantly more complex system and represents a broader challenge with barriers including paucity of safety champions and leadership, individual clinician autonomy competing with teamwork, and multiple opportunities for communication breakdown.(3) These challenges are further accentuated in times of recession and tightening health budgets when the challenge of compliance with targets can divert focus from safer systems. The Mid Staffordshire Trust in the UK’s National Health Service (NHS) was a high performing trust according to its statistics but suffered system wide failings in patient care and safety. The 2010 Francis inquiry into the Trust found that a focus on targets and financial reporting to multiple bodies occurred to the detriment of patient care and staff wellbeing.(81)

1.4.1 A safety culture
A systems approach to patient safety requires a shift from a blame culture, which incentivises people to cover up, to a systems-based safety culture. A safety culture is an organisation’s culture with respect to safety – its attitudes, beliefs and practices. In a blame culture the main objective is to identify the healthcare professional who performed the unsafe act(s) which caused the adverse event. That person is then named, blamed, shamed and disciplined. This isolates the individual from the system but not the conditions in the system which allowed the event to occur.(82)

In a safety culture efforts to correct errors target system factors rather than “blame” the individuals involved, unless the action was deliberate. In this way a safety culture is a just culture and can differentiate between those who are blameless and those with blameworthy actions (honest errors compared to unacceptable unsafe acts).(77) There is therefore a balance between no blame and the responsibility of individuals to be part of the safety culture (which encourages members to follow guidelines and best practice, undergo
training, etc.). This individual accountability is necessary to successfully implement safety strategies.(83) A safety culture is also a reporting culture (reporting and collecting information on adverse events and near misses) and a learning culture (the ability to learn from past events).(82)

However, despite the growth of knowledge about patient safety, investigations continue to highlight the need for cultural change in healthcare. The 2010 Francis report into Mid Staffordshire Foundation Trust called for “fundamental culture change”, including openness and a change from a blame culture to one of safety.(81) Ongoing barriers to the adoption of a safety culture include the idea of “trained perfectibility” (the concept that medical training is sufficient to create perfect clinicians able to practise without error) and the hierarchical nature of healthcare professions and systems. These result in fallibility being stigmatised and sanctioned because error is considered a sign of incompetence, therefore making it difficult to admit to error or to learn from collective errors.(82) Essential to a safety culture are clear organisational goals and leadership in patient safety; these have been shown to result in greater patient satisfaction.(84)

1.5 Patient safety in the Republic of Ireland

1.5.1 Healthcare in the Republic of Ireland
Healthcare in the Republic of Ireland is a public-private mix. Public healthcare services are provided by the HSE. Under the Health Act 2004, the HSE is required “to manage and deliver, or arrange to be delivered on its behalf, health and personal social services”.(85) The Department of Health provides strategic leadership for the health service and implements government health policy.(86)
Hospital beds in Irish public hospitals are paid for by the State (fully for holders of medical cards, or partly – non medical card holders without private health insurance contribute out-of-pocket supplements) or by private health insurance. There are currently 11,660 public hospital beds in the Republic of Ireland and nearly 4,400 private beds (2,461 in public hospitals and 1,926 in private hospitals). (87) Approximately 45% of the population had private health insurance in 2013. (85)

Consultations with general practitioners (GPs) are fee-for-service or, in selected cases, state funded via the medical card and GP visit card. Medical card holders have access to free GP consultations, hospital services, subsidised medication, certain dental, ophthalmic and aural services, and some personal and social care services (public health nursing, social work and community care services) based on need. Eligibility for the medical card is based mainly on means but can also be allocated on a discretionary basis due to clinical need or where access is ‘unduly burdensome’. Forty percent of the Irish population in 2013 were medical card holders. (85) Another 3% had GP visit cards. GP visit cards entitle the bearer to free GP consultations and are also means tested (higher thresholds) with some discretionary allocation as previous. (85) The government is currently expanding its free GP visit scheme and in 2015 this was extended to everyone in the population aged under six or over 70 years (on application). For those without a medical card there is a part charge for hospital services (emergency department visits and a daily in-patient charge) and they are charged the full fee-for-service cost by the GP (unless they have a GP visit card).

1.5.2 Patient safety structures in the Republic of Ireland

1.5.2.1 Quality and Fairness

The HSE was established in January 2005 as the single body responsible for meeting Ireland’s health and social care needs. (88) Prior to this, healthcare services were delivered through a range of different agencies, each of which
was independently answerable to the Department of Health and Children (now referred to as the Department of Health).(88) This diversity made it difficult to provide nationally consistent health services. Reform of these structures, in particular the acute hospitals, was a key component of the 2001 National Health Strategy *Quality and Fairness*.(89) Provision of standardised quality systems to support best patient care and safety was one of the national objectives of the strategy.

### 1.5.2.2 Clinical Indemnity Scheme
The *Quality and Fairness* strategy also heralded the creation of the CIS and the Health Information and Quality Authority (HIQA). The CIS was established within the State Claims Agency in 2002 to manage all clinical negligence claims relating to professional clinical services in the Irish public health sector.(90) To assist with this a national clinical incident reporting system was rolled out in 2003.(88, 90) This confidential web-based electronic incident reporting system for healthcare providers was initially known as STARSweb.

### 1.5.2.3 Health Information and Quality Authority
HIQA was established in 2007 under the *Health Act 2007*. It is an independent State body charged with setting standards on the safety and quality of health and social services and to monitor healthcare quality via enforcement of these standards. It undertakes investigations into safety, quality and standards of the health services if the Authority believes on reasonable grounds that there is a serious risk to the health or welfare of a person receiving those services. There have been several high profile HIQA investigations into patient safety following tragic incidents in Irish hospitals.(91, 92)
1.5.2.4 Department of Health and the Madden Report

The Patient Safety and Quality Unit of the Department of Health, provides the policy lead on patient safety and healthcare quality. (93) This unit is responsible for monitoring implementation of the recommendations of the Commission on Patient Safety and Quality Assurance. The Commission was set-up in January 2007 “to develop clear and practical recommendations which would ensure the safety of patients and the delivery of high quality health and personal social services would be paramount within our health service”. (88) Part of the drive for a Commission was the investigation into peri-partum hysterectomies at one Irish hospital and the realisation that national as well as local policy change would be required to address the identified failings in healthcare. (94) The Commission’s report *Building a Culture of Patient Safety* (also known as the Madden report) was published in 2008. (88)

The Patient Safety First initiative was launched by the Patient Safety and Quality Unit in 2010 to implement the recommendations of the Commission. The Patient Safety First declaration was signed by the then Minister for Health, healthcare leaders and service users committing “organisations to according the highest level of priority to patient safety”. (95) The website promotes awareness of patient safety developments in Ireland and provides a repository of information on patient safety in Ireland with links to HSE and HIQA work in the area. It is difficult to tell from the website whether the Patient Safety First initiative is ongoing. Most of the current initiatives date to 2010 or earlier. There is a link to the 2015 National Patient Safety Conference but otherwise no evidence of recent activity. In addition, the Commission’s recommendation to develop a Patient Safety Agency is “under review in the context of the strategic reform of the health services and the measures that are being taken to strengthen patient safety, including advocacy and related services, within the HSE.” (96)
1.5.2.5 HSE Quality

The Office of Quality and Risk was created within the newly formed HSE in 2005. In this, safety and safety standards were a component of risk management.(89) More recently, 2011 saw the establishment of the Quality and Patient Safety Directorate within the HSE. This Directorate had the objective of providing leadership and support to the HSE in delivering high quality and safe services to patients, their families and members of the public.(97) Currently, in 2015, the HSE is separating its quality improvement and patient safety functions as part of a Quality and Patient Safety Enablement Programme.(98) The Directorate will become the Quality Improvement Division and patient safety (incident management and serious reportable events) will be incorporated into the Quality Assurance and Verification Division under its performance measurement function.(98)

1.5.2.6 National initiatives

Other national activities in the Republic of Ireland relevant to patient safety include the National Clinical Effectiveness Committee, Clinical Programmes and Clinical Governance initiatives. The National Clinical Effectiveness Committee was established as part of the Patient Safety First initiative in 2010. Its role is to prioritise and quality assure clinical guidelines and clinical audit. This work will develop a suite of National Clinical Guidelines.(99)

The National Clinical Programmes were established between 2009 and 2010 to improve and standardise patient care throughout the health system by bringing together clinical disciplines and enabling them to share innovative solutions to deliver greater benefits to health service users. The Programmes are based on three main objectives: improving the quality of care delivered, improving access to all services, and improving cost effectiveness.(100) There are currently 33 Clinical Programmes in operation including: acute medicine, chronic obstructive pulmonary disease, elective surgery, stroke, medicines management and radiology. Each programme is governed collaboratively by the relevant specialty professional body and the HSE, and
run by a multidisciplinary working group. Each programme has a set of aims and key deliverables each year. The aim of the elective surgery programme, for example, is to improve the patient’s elective surgical journey through better access, defined pathways, better processes and monitored clinical outcomes. Tangible deliverables include the reduction of average length of hospital stay for surgical patients, the implementation of a national surgery audit programme and the implementation of the productive theatre improvement programme (as developed by the NHS innovation) aimed at improving theatre utilisation.

The Quality and Safety Clinical Governance Initiative was established in 2012. It is a framework through which healthcare teams are accountable for quality, safety and patient satisfaction in the care they deliver. It is built on a partnership model of healthcare management with clinical directors/leaders. (101)

1.5.3 Adverse event reporting in the Republic of Ireland
The Commission on Patient Safety and Quality Assurance report Building a Culture of Patient Safety acknowledged the existence of the national incident reporting system within the CIS but stated that there was no universal system that captured adverse event data from all elements of the health sector. (88) It recommended the development of a national mandatory reporting system for adverse events that result in death or serious harm and for this system to be able to collect voluntary reports of a less serious nature. (88) Implementation of this recommendation is still underway. It appears that it will be achieved via two linked systems: incident reporting through the CIS and the development of the HSE “Reportable and Serious Reportable Events” system.
The CIS receives reports of adverse clinical incidents from publicly funded healthcare organisations through a web-based information technology system that links healthcare organisations to the CIS central database, held in the State Claims Agency. (90) The system was migrated from STARSweb to the National Incident Management System (NIMS) in 2014, and in 2015, the name changed to the National Adverse Events Management System (NAEMS). It is designed to capture all clinical incidents and near misses. The adverse event reporting form is not anonymised in terms of the patient or the reporter (Appendix 1). It is not clear from the State Claims Agency website in what form the HSE and HIQA receive information from this reporting system.

The NAEMS is intended to support local risk management initiatives and enable national trend analysis. There is a statutory requirement for public sector organisations run by the HSE to report, but primary care and private healthcare are not obliged to report.(88) Each year the CIS publishes a brief summary on the “Key figures” page of its website of the previous year’s adverse events and closed claims. At the time of writing this thesis, only the 2014 closed claims figures were available.(76)

Initiatives are currently being undertaken in the HSE and CIS to streamline the collection and investigation of events resulting in death or serious harm.(98) These include completion of an additional incident form for NAEMS when an incident satisfies any of the Serious Reportable Event (SRE) list of clinical scenarios (Appendix 2) or otherwise needs to be notified to management. This data will be collected as part of the ‘Reportable and Serious Reportable Events’ system in the HSE.(102) Prior to this new system, it appears these types of incidents were notified to the CIS via a rapid notification system (in addition to routinely through STARSweb), that also notified the Claims section of the State Claims Agency.(90) Again, it is not clear how, or whether, the HSE or HIQA were included in this correspondence.
Healthcare-related incidents are also collected by other organisations in the Republic of Ireland, including: the Health and Safety Authority (work-related incidents); the Healthcare Products Regulatory Authority (medicine-related adverse reactions, medical device-related adverse incidents, blood/tissue/cells-related adverse events); the coroner (32 instances in which deaths must be reported); HIQA (notifiable events occurring in residential services for older persons, serious incidents and deaths in children in childcare); the Health Protection Surveillance Centre (communicable disease); Maternal Death Enquiry (maternal deaths); the Medical Exposure Radiation Unit (radiation incidents to patients); the Mental Health Commission (deaths in approved mental health centres), National Perinatal Epidemiology Centre (stillbirths and neonatal deaths); the National Haemovigilance Office (severe adverse reactions/events relating to blood components); and the Radiation Protection Institute of Ireland (radiation incidents to staff).(102)

All of these reporting systems have variations in incident definition and criteria for reporting and have separate data collection systems. For example, the Health and Safety Authority defines an adverse event as “any event or circumstance which could have or did lead to actual or possible personal injury, personal harm, property damage or loss”,(103) and the Healthcare Products Regulatory Authority defines a medicine-related adverse reaction as a “response to a medicinal product which is noxious and unintended”, including “any harm associated with the use of a medicine, use following overdose, misuse or error”.(88, 104)

1.6 Measuring adverse events
There is no gold standard for measuring adverse events. Clinicians use mechanisms such as morbidity and mortality conferences (i.e. internal meetings), autopsies, discrepancy meetings (where misdiagnosis cases are discussed), risk and outcome registries and audit to evaluate practice and identify errors. Hospitals routinely report their performance with
organisational administrative statistics, including waiting times, readmission and mortality rates, and the annual numbers of patient complaints, claims or incidents. However, such data do not indicate the degree of safety or rate of occurrence of medical harm in an organisation and provide only a partial view of the problem. Morbidity and mortality conferences and other forms of incident reporting have been shown to miss 65% - 91% of adverse events, and large outcome studies and registers do not separate out events caused by healthcare management from disease progression.

In contrast, evaluation of safety requires the systematic measurement of adverse events in a population. Use of accurate and standardised data and systematic investigation of adverse events can provide information on incidence and can demonstrate areas of risk and preventability that are amenable to action. Targeted measurement of adverse event rates over time can evaluate whether improvements are occurring. Adverse event data can then be used to highlight patient safety issues that require addressing at an organisational level and inform local and national patient safety policy.

Adverse event rates can be calculated in many different ways using a variety of data sources including incident reporting, review of patient charts, electronic administrative databases (e.g. discharge codes), patient complaints or malpractice claims data, interviews of clinical staff or prospective reporting by clinical staff, and clinical surveillance (observation of patient care or examination of patients). These methods are discussed below.
1.6.1 Incident reporting

Healthcare organisations often require all incidents (including near misses) of patient harm to be reported for their quality and safety monitoring. This system of reporting is known as incident reporting. If the incident is very serious, or could have been very serious, an organisation may want these highlighted for investigation. These incidents may be called serious reportable events, sentinel events or never events.\(^{102}\)

Multiple studies have shown that existing incident reporting collects only a small proportion of adverse events (approximately 3% - 10%) and are not representative of all adverse events.\(^{34, 108, 110}\) For example, the majority of incident reports are falls, pressure ulcers and drug-related events; whereas these constitute a minority of adverse events detected by patient chart review (70% versus 26% in one comparative study\(^{108}\)). Doctors are less likely to report than nurses and the professions report different types of events.\(^{60}\) A survey of midwives and doctors in an obstetric unit found that reasons for not reporting included fear that junior staff would be blamed, workload, “extenuating” circumstances, and concern about litigation.\(^{114}\) Additional methods over and above incident reporting are therefore required to adequately assess the incidence and prevalence of adverse events in healthcare.

1.6.2 Electronic data

Existing electronic data (e.g. admission or discharge clinical coding, private healthcare billing data) may be searched for adverse events with the benefits of being able to assess large numbers of patients/admissions and compare across different healthcare settings which collect similar data. However, this data (usually collected for other purposes than detection of adverse events) is dependent on the accuracy of the coding system and limitations of the coding dictionary for diagnostic information.
The use of electronic data in adverse event detection is hampered by relatively poor sensitivity and specificity. (115) This was demonstrated in a patient chart review study of adverse events in Boston which compared screening with electronic billing data versus traditional chart review using a list of triggers. The electronic data (readmission, death, transfer to a special unit, return to the operating room and transfer to another hospital) allowed the identification of 173 out of the 339 adverse events identified through traditional two-stage chart review, and had a sensitivity of 47% and specificity of 74%. In contrast, chart review had a sensitivity of 93% and specificity of 42%. (18) Furthermore, electronic data has the disadvantages that it does not engage the clinicians at the time of the healthcare delivery and is unable to determine preventability or system factors. (115)

To improve the utility and standardisation of electronic search methods, the Agency for Healthcare Research and Quality in the United States developed a list of diagnostic codes that were indicators of adverse events. Preliminary work adapted some of these for use with NHS admissions data. (109) The authors found that admissions with these codes had higher mortality, length of stay and readmission rates. There was, however, substantial variability between NHS trusts and it was not clear whether this was due to variations in secondary diagnosis coding or quality of care. (109)

In the future a combination of electronic data searching and chart review could result in a more efficient version of the Harvard Medical Practice Study method, especially with the advent of electronic health records. (115) Alternatively it could be used for non-comprehensive case finding and qualitative analysis rather than systematic adverse event reporting. (116)
1.6.3 Claims and complaints data
Claims data provides a depth of information about the adverse events that are investigated. However, only a small proportion of adverse events are potentially compensable and therefore likely to result in a claim. In the NZ adverse events study just over 2% of the adverse events were associated with a compensable adverse event.\(^{117}\) This was similar in a comparison of the adverse events from the Dutch patient chart review study with claims and complaints data – only 1.8% of chart review adverse events were captured in the claims and complaints data. When incident reporting was added, this figure only increased to 3.6%.\(^{110}\)

1.6.4 Retrospective patient chart review
Retrospective patient chart review involves review of patient charts after discharge. There are two main methods and both use a trigger tool to screen for charts with potential adverse events: the Harvard Medical Practice Study methodology and the Global Trigger Tool (GTT). Chart review is seen as a sensitive method to detect adverse events but the retrospective design is subject to hindsight bias. Hindsight bias occurs when knowledge of the outcome of the event and its severity influences the assessment of causation and preventability. It is particularly an issue for preventability.\(^{118}\)

1.6.4.1 Harvard Medical Practice Study
The Harvard Medical Practice Study methodology employs retrospective chart review and this approach is the standard methodology used in a number of international studies.\(^{2}\) It is sensitive in detecting adverse events and has become the benchmark for measuring adverse events in hospitals and healthcare systems.\(^{119}\) This approach involves a two-stage patient chart review: in stage one reviewers screen patient notes for 'triggers' from a list of scenarios that may indicate an adverse event has occurred (e.g. unplanned admission to intensive care, unexpected death, etc.) followed by stage 2 physician review of 'triggered' charts for any adverse event using a
standard definition (an injury resulting in disability at discharge, prolonged hospitalisation, or death, caused by healthcare management).(2)

The Harvard Medical Practice Study was based on a 1974 Californian study examining the feasibility of an alternate method of compensation and insurance than the tort law system. The Californian study examined patient charts for disability resulting from healthcare management in a representative sample of in-patients in California and a potentially compensable event was defined as “disability caused by healthcare management”.(120) The Harvard Medical Practice Study, also examining issues of compensation and insurance in New York, was the first to coin the term adverse event. In order to be classified as an adverse event all three of the following conditions had to be met: injury caused at least in part by medical management; must have measurable disability that prolonged the hospital stay or reduced function at the time of discharge; and it must have been unintended.(121) The Harvard Medical Practice Study tool was reoriented in the Australian study from a focus on negligence (was care substandard?) to quality (was the adverse event preventable?).(2, 30, 122)

The Harvard Medical Practice Study performed extensive testing of its methodology. In a pilot study the investigators compared chart-identified adverse events with risk management and litigation records and found that the chart review missed 3.4% of cases in these records because of missing information. Four percent of charts were unable to be accessed, so they performed an analysis of administrative data (age, specialty, diagnosis) from the 4% of missing records to ensure there was no selection bias. The authors also determined the frequency of missed adverse events with the trigger screening and found a false negative rate of 7.9% (litigation and risk management records were the gold standard). By using a 5% prevalence of adverse events (based on the Californian study) the sensitivity of the stage one screening was calculated as 80%. In the triggered charts, 12.6% of adverse events were not discovered by physician review. Most of the
adverse events that were missed were the less serious ones. They used this data to provide an estimated retrieval rate of 78% for the method (100 x 0.966 [3.4% rate of missed AEs due to insufficient information in charts] x 0.921 [7.9% false negative rate in screening process] x 0.874 [12.6% rate of missed AEs when information was in the chart]). However an additional 11.6% of events discovered by chart review were not in the litigation and risk management records, so the true retrieval rate of adverse events is likely to be higher. (121)

This method has been criticised for its reliance solely on documentation (though use of written history can also be considered an advantage), high cost, focus on individuals rather than systems, and difficulty in assessing retrospectively the contributions of disease processes compared with healthcare management. The determination of an adverse event is based on implicit structured review of the chart and has been criticised for variation between reviewers and moderate kappa estimates. (123, 124) It can also be difficult to judge preventability and examine underlying system factors responsible for particular events. (125) Although expensive to have charts reviewed by professionals, an advantage of retrospective chart review is that it does not impact on clinical work. (125)

This method has not been thought of as optimal for assessing the impact of interventions to reduce adverse events due to the expense of conducting large reviews and the broad range of events collected. (125) Nonetheless, a group from the Netherlands repeated a national study three times providing longitudinal data over eight years. (15, 126) There was an increase in adverse event rates between the first two time periods, which stabilised in the final study. (126) Although, the preventable rate reduced by 45% over the period of the three studies, this became a non-statistically significant 30% reduction after weighting of the data for the sampling strategy. The authors concluded that the challenge of adverse events remains but some progress may be inferred, which they ascribed to several national safety
Accompanying editorials agreed that this method of adverse event measurement is useful for demonstrating burden but more targeted approaches are required for evaluating specific quality initiatives. (123, 127)

### 1.6.4.2 Global Trigger Tool
The Global Trigger Tool was developed by the Institute for Healthcare Improvement as a less labour intensive method of chart review (than the Harvard Medical Practice Study) to identify adverse events. It was intended as a tool to direct resources and measure trends over time. All events that result in harm are included, with harm defined as “unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment or hospitalization, or that results in death”. Preventability is not assessed. Small samples of ten patient records are randomly selected from the population of discharged patients every two weeks to generate two data points each month. (128)

The first phase involves two primary reviewers independently screening selected charts. A larger list of triggers is utilised than in the Harvard Medical Practice Study. When a positive trigger is found the reviewer reviews only the pertinent section of the chart for that adverse event. If no event is found the reviewer proceeds to evaluate the presence of the next trigger until 20 minutes elapses and reviewing stops. The tool is not meant to identify every adverse event. The two primary reviewers meet and come to a consensus which is documented on a summary sheet. This is reviewed by the physician reviewer for final arbitration on the presence of an adverse event.

A small number of charts are reviewed at each interval enabling change to be tracked over time. The Global Trigger Tool is not designed to assess preventability (though this was included in a Danish implementation study using a separate tool). (129) It does not assess additional length of stay and
the full chart is not reviewed by the primary reviewer or the physician
reviewer. Consistency between reviewers is also a methodological concern
with the Global Trigger Tool.(130)

The Global Trigger Tool employs a broader definition of adverse events (i.e.
it includes harm occurring during the admission which resolved prior to
discharge) than the Harvard Medical Practice Study and has identified higher
rates of adverse events than the Harvard methodology (20 - 30%).(116)
However, in a direct comparison using the same criteria for defining adverse
events, the Harvard Medical Practice Study methodology was found to be
slightly more sensitive.(116) In the future, as with the Harvard study,
automation of the Global Trigger Tool with the electronic health record may
further enhance its utility for healthcare organisations.(116)

1.6.5 Prospective adverse event capture
The prospective collection of adverse event data involves researchers or
clinicians at the clinical interface identifying adverse events as they occur.
This may entail any combination of chart review, electronic searches,
interviewing patients and staff, direct observation on the ward, and clinical
examination of patients. Prospective adverse event determination is less
prone to recall bias than retrospective methods. It provides better
assessment of the clinical context and chain of errors and also enhanced
identification of adverse events that are poorly documented in written notes
(for example pain and psychological distress).(21) This aids in the
determination of preventability and studying system factors. However,
prospective collection is an additional task for frontline staff,(125) although
this can also be seen to be an advantage, as by including staff the dynamic
alters such that healthcare professionals are no longer seen as targets (in
the chart review approach) rather as participants in the adverse events
process (through self-reporting).(22) This method can assist in education of
healthcare professionals about patient safety by showing them that errors
can result in adverse events.(21)
1.6.6 Cross-sectional adverse event capture

Cross-sectional collection of adverse events involves the capture of events at one time point during the admission. This may involve interview of clinical staff or patients, or use of electronic data, with or without review of patient charts. It is considered a less expensive design than retrospective chart review or prospective collection involving repeated visits to wards. This method has the advantage that staff on site can be questioned and therefore is less dependent on the quality of the patient chart. Cross-sectional collection underestimates adverse events related to admissions because it does not capture events that occur in the admission after data collection or prior to the start of the defined time point.

1.6.7 Prospective, cross-sectional and retrospective methods compared

In preparation for a national study in France, Michel and colleagues compared capture of adverse events through patient chart review using cross-sectional, prospective and retrospective data collection and identical forms. They found that prospective and retrospective methods identified similar numbers of adverse events (70% and 66% of the combined total adverse events) but cross-sectional discovered one-third fewer. The cross-sectional design also identified more false positives and none of the most serious events. The prospective method identified 24% more preventable (64% versus 40%) events than retrospective collection and was significantly more effective in detecting adverse events in medicine. The retrospective method was better than prospective collection at capturing events occurring in surgical specialties but this did not reach statistical significance. The work load was similar for the ward staff for both prospective and cross-sectional methods (about three hours on the first ward visit, no further visits for cross-sectional and quicker visits subsequently for prospective as the patients had been identified). The workload for ward staff was much less for retrospective. Ward staff preferred the prospective method because it had more face value and was of benefit in terms of learning and communication about adverse events.
being the most expensive (by 20%), its advantages in terms of preventability and staff engagement resulted in it being used for the subsequent French national study. (21)

O’Neil and colleagues in a Boston hospital adverse events study also compared the Harvard Medical Practice Study two-stage retrospective chart review method with prospective physician reporting plus chart review. (22) They found similar adverse event rates (2.7% and 2.8%) with the two methods but prospective reporting identified more preventable events (62.5% versus 32%) and was less costly. The authors noted that, although the rates were similar, the methods did not necessarily capture the same events, indicating that the true adverse event rate could be higher than either estimate alone. Both methods were equally as good at identifying events occurring prior to the index hospitalisation or during the admission and serious events. Prospective reporting captured more errors of commission than retrospective chart review. This study compared both methods with existing voluntary reporting systems and found voluntary reporting to miss large numbers of events discovered by the other two methods. (22)

1.6.8 Reliability of adverse event determination

Most adverse event capture methods, e.g. review of patient charts, voluntary reporting, or capture of claims data, require a reviewer or a reporter to determine the presence of an adverse event. In most cases the event is judged against the definition of an adverse event. It is not possible to create a list of criteria for every adverse event and thus assessment of causation and preventability involve implicit judgements by a reviewer. Methods involving reviewers assess consistency of application of these judgements through the use of independent double review and calculation of the kappa statistic. To enhance consistency, methods determining adverse event rates use standard training and structured assessment forms. (121)
1.7 An Irish baseline national study of adverse events

In the Republic of Ireland, despite a number of investigations into tragic incidents,(91, 92) there is no national data on the incidence and prevalence of adverse events. Therefore, recommendations on how to enhance patient safety at a national level are being made on limited information.

The first patient safety research question to be addressed in any healthcare setting is the extent and nature of the problem. Although there have been several large prevalence studies internationally, the WHO recommends collecting local national incidence and prevalence data.(131) This is because such information has been shown to provide the mandate and commitment for patient safety action within a country. For example, in Canada, the publication of their first national adverse events study helped to launch the Canadian Patient Safety Institute.(132) In the Netherlands, their national study results provided the impetus for a national patient safety action campaign in hospitals "Prevent harm, work safely".(31) The aim of collecting local data from hospitals in the Republic of Ireland is to provide robust baseline data to demonstrate conclusively the extent and nature of the problem of medical harm in the Irish hospital system and provide policymakers with an evidence base with which to take action to improve patient safety.

Before the Harvard Medical Practice Study method was chosen for the Irish National Adverse Events Study, the essential characteristics of each method were considered for their suitability for a baseline national adverse events study (Table 1.1). Critical for a baseline national study is that the method of determining adverse events should have high sensitivity and be able to assess preventability, and therefore has the ability to produce recommendations for intervention and further research. This method should be the "gold" standard in the field and enable comparison with other jurisdictions. Characteristics such as involvement of frontline staff, ability to assess local system factors or track adverse events are desirable but were
deemed more important for local adverse event data collection compared with the requirements of a national study.

<table>
<thead>
<tr>
<th></th>
<th>Incident reporting</th>
<th>Electronic discharge diagnoses</th>
<th>Claims data</th>
<th>Prospective capture at the clinical interface</th>
<th>Retrospective chart review using trigger tools</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HMPS</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Timely</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Low cost</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Information collected on entire population</td>
<td>X</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Low impact on clinical workload</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Ongoing local tracking</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Large national studies</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓ (many)</td>
</tr>
<tr>
<td>Assess preventability</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Assess system factors</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>“Gold” standard</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
</tbody>
</table>

The Harvard Medical Practice Study methodology has been shown to have high sensitivity in adverse events detection and can determine preventability. While there is no “gold” standard for adverse event measurement, this method has been used by a number of seminal national prevalence studies enabling international comparisons. For the Irish National Adverse Events Study, the methodology was based specifically on the Canadian Adverse
Events Study, which employed a modified protocol of the Harvard Medical Practice Study. (2, 16) The advantages of this decision will be discussed further in Chapter 3: Methods.
1.8 Aims and objectives of the thesis

1.8.1 Aims
The primary aim of this thesis was to quantify the frequency and nature of adverse events in acute hospitals in Ireland using an internationally recognised, retrospective, patient chart review methodology. Secondary aims were to characterise risk by specialty and patient characteristics, establish the rate of preventable adverse events, determine the cost of adverse events, and compare the INAES adverse event rates with incident reporting and those obtained in other international studies.

1.8.2 Objectives
1. What is the frequency and nature of adverse events for adult patients in major acute hospitals in Ireland?
2. How does the frequency and nature of adverse events for adult patients vary between the medical and surgical specialities in acute hospitals in Ireland?
3. What risk factors are associated with adverse events in major acute hospitals in Ireland?
4. What proportion of adverse events identified by retrospective case note review is also identified by incident reporting?
5. What is the rate of preventable adverse events in Ireland?
6. What is the cost of adverse events to the Irish healthcare system?
7. How does the Irish rate of adverse events compare with other international retrospective chart review studies?
8. Based on the key findings arising from the thesis, provide recommendations for dissemination of the results into policy, practice and research.
1.9 Conclusion

Patient safety came to prominence after the publication of the *To Err is Human* report in 1999. This led to the development of the systems approach and promotion of a safety culture in healthcare. Large adverse event studies reviewing hospital patient charts have estimated that adverse events occur in between 3% and 17% of admissions, with one- to two-thirds of these being preventable. Most adverse events are mild but approximately 14% cause permanent harm or contribute to death. Adverse events result in longer hospital stays and are a substantial cost to the healthcare sector. Adverse events are captured through a variety of methods but only systematic collection in a population can be used for healthcare quality reporting of adverse events. This is not being achieved in the Republic of Ireland currently and there is no national information on the incidence and prevalence of adverse events. The Harvard Medical Practice Study retrospective methodology of two-stage patient chart review was chosen for the Irish National Adverse Events Study due to its high sensitivity, use in other international studies and ability to assess preventability.
2 CHAPTER 2: A systematic review of adverse event studies

2.1 Background
The Irish National Adverse Events Study Working Group identified the Harvard Medical Practice Study methodology for this first Irish study of hospital-based adverse events. An important justification for this was that the existing international literature of adverse events in hospital settings predominantly used this methodology.

One of the objectives of this thesis was to compare the Irish rate of adverse events with other international retrospective chart review studies. A systematic review of adverse event studies by de Vries and colleagues (35) was published in 2008; however, this does not include more recent studies. Therefore, in order to achieve this objective, a systematic review was performed to extract all international retrospective chart review studies and the methodologies they used.

Another objective of this thesis was to determine the risk factors associated with adverse events. However, the main publications from international adverse event studies contain little information about the patient characteristics (e.g. demographics, socio-economic factors, co-morbidity) associated with increased adverse event risk. Instead, results focus on hospital environment factors such as type of admission, location of adverse event, responsible specialty. Therefore, the systematic review also sought to identify information about patient characteristics associated with adverse events by including all publications, as well as the main results publication, for each adverse events study.
2.2 Objectives

The objectives of the systematic review were to:

- Systematically review the literature for studies of adverse events in adult in-patients in acute hospitals
- Compare adverse event studies in terms of their setting and methodology
- Determine the patient characteristics which are associated with an increased risk for adverse events in adult in-patients.

2.3 Methods

I undertook the systematic review with a medical student (FH). The search strategy was developed jointly with the assistance of a librarian. FH performed the electronic searches. FH and I independently screened the titles and abstracts of all records identified by the searches, the full texts of potentially eligible publications and extracted data on adverse event frequency and patient risk factors from the included publications. FH and I performed the qualitative synthesis of the patient characteristics data. I extracted data on each study’s methods and undertook the qualitative synthesis of this information. I developed the list of variables to be extracted.

2.3.1 Eligibility criteria

In order to compare adverse event rates and characteristics of patients with adverse events, all studies must have used the same adverse event definition. The definition chosen for the systematic review was therefore the one used in the Harvard Medical Practice Study methodology and this was in line with that used in the de Vries systematic review.(2, 35)

Studies were included if they were studies of adverse events in adult in-patients in acute hospitals and defined an adverse event as follows: an unintended injury or complication resulting in prolonged hospital stay,
disability at the time of discharge or death, and caused by healthcare management rather than by the patient’s underlying disease process. (2) Therefore, all studies which used this definition (or similar) to evaluate the incidence of adverse events in adult in-patients were eligible for inclusion.

2.3.2 Literature search
A formal literature search of MEDLINE (January 1980 to June 2015), Embase (January 1980 to June 2015), CINAHL (1982 to June 2015), PsycINFO (1967 to June 2015) and Cochrane (up to June 2015) was conducted. Appropriate search strategies were developed with the assistance of a librarian and based on the de Vries systematic review. (35) Search strings utilised both key words and MeSH terms in order to maximise sensitivity of the search. Keywords used were “Harvard Medical Practice”, “adverse event”, “iatrogenic injury” and “medical error”. MeSH terms used were “patient harm” and “iatrogenic disease/complications”. An example of a MEDLINE search string used was: ((((((((("harvard medical practice") OR ("adverse events") AND preventable)) OR ("adverse event") AND preventable))) OR ("iatrogenic injury") AND "preventable"))) OR ("iatrogenic injuries") AND preventable)) OR ("medical errors") AND preventable)) OR ("medical error") AND "preventable) OR patient harm[MeSH Terms]) OR iatrogenic disease/complications[MeSH Terms]) The full search is detailed in Appendix 3. Additional relevant studies were identified by hand-searching references of retrieved publications.

2.3.3 Study Selection
All studies of adverse events in adult hospital in-patients were considered. Studies that evaluated specific types of adverse events (e.g. medication errors only) or studies that investigated specific patient populations (e.g. psychiatric patients, intensive care patients only) were excluded. Where an article was in a non-English language, the author was contacted by email to see if there was an English version available. If not, the article was excluded from the study.

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2.3.4 Quality Assessment

The quality of reporting of the included adverse event studies was assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, a tool for analysing the quality of observational studies. (133) The STROBE statement is referred to in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors. The Statement employs a checklist of 22 items that relate to the title, abstract, introduction, methods, results, and discussion sections of publications. Publications are given a score out of 22, with 22 indicating the highest quality according to the checklist. Two STROBE checklists were completed for the main results paper for each adverse events study. FH and I completed the checklists independently, with the final score obtained through consensus.

2.3.5 Data extraction and synthesis of results

FH and I extracted data on the occurrence of adverse events from the main results publications.

I extracted data on study methodology. The following information was obtained: setting, number of hospitals/ records, method, sampling, sample population, adverse event review period and timing, reviewer (number and inter-rater reliability kappas), trigger list, healthcare management causation and preventability levels.

Data on patient characteristics that were examined for adverse event risk were independently extracted by both FH and I from each eligible adverse events study (the main results paper and any associated publications of data from the same study). The following information was obtained: sex, age, ethnicity, socioeconomic status, co-morbidity. Adverse event risk was considered to be associated with a characteristic if the authors stated that an association had been found and/or data was presented with a measure of
association indicating a statistically significant difference. The data was collated and cases of disagreement were resolved by consensus.

Qualitative synthesis was performed on the data extracted.
2.4 Results

A flow diagram of the literature identified in the systematic review is presented in Figure 2.1.

*different definition of an adverse event (n=26), not an adverse events study (n=13), English version of full-text unavailable (n=7), conference abstract only (n=5), other study design (n=5), duplicate/reprint (n=5), study outcome not adverse events (n=4), wrong patient population or setting (n=4)

Figure 2.1 Systematic review flow-chart
The search yielded 4201 publications, of which 2867 were excluded after reviewing titles and abstracts. Of the remaining publications, 69 were excluded after reviewing the full text for the following reasons (number excluded given in brackets): different definition of an adverse event (n=26), not an adverse events study (n=13), English version of full-text unavailable (n=7), conference abstract only (n=5), other study design (n=5), duplicate/reprint (n=5), study outcome not adverse events (n=4), wrong patient population or setting (n=4). Five additional publications were retrieved by hand-searching bibliographies.

Fifty-four publications were included in the systematic review. These represented 25 separate adverse event studies with 29 associated publications containing additional analyses of data from the main adverse event study (Table 2.1). Nine adverse event studies had associated publications; the highest number of associated publications was seven.
Table 2.1 Publications reviewed for each adverse events study

<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Strobe score out of 22</th>
<th>Associated publications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>20.5</td>
<td>Leape 1991(11)</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>20.5</td>
<td>Bates 1995(18)</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>21.5</td>
<td>Wilson 1999(134)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kable 2002(36)</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>20.5</td>
<td>Thomas 1999(74)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gawande 1999(41)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thomas 2000(135)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thomas 2000(26)</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>19.0</td>
<td>Woloshynowycz 2000(136)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neale 2001(137)</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>17.5</td>
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<td></td>
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<td>Forster 2004(19)</td>
<td>18.5</td>
<td></td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>16.5</td>
<td></td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>20.5</td>
<td></td>
</tr>
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<td>Sari 2007(23)</td>
<td>21.0</td>
<td>Sari 2006(108)</td>
</tr>
<tr>
<td></td>
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<td>Michel 2007(21)</td>
<td>18.0</td>
<td></td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>21.5</td>
<td>Aranaz-Andres 2009(141)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aranaz-Andres 2011(13)</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>22.0</td>
<td></td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>18.5</td>
<td>Martins 2011(142)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mendes 2013(50)</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>21.5</td>
<td>Smits 2010(143)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hoonhout 2009(73)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hoonhout 2010(47)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zwann 2010(45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zegers 2011(42)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zegers 2011(40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Merten 2013(144)</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>17.0</td>
<td></td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>21.0</td>
<td></td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>18.5</td>
<td></td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>21.0</td>
<td>Baines 2013(145)</td>
</tr>
<tr>
<td>Sommella 2014(24)</td>
<td>17.5</td>
<td></td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>18.5</td>
<td></td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>21.5</td>
<td></td>
</tr>
</tbody>
</table>
2.4.1 STROBE scores
The STROBE checklist scores for the main results paper from each study ranged from 16.5(125) to 22 out of 22(33) (Table 2.1). The most common criteria missing were a full description of the methodology in the title of the paper, a sample size calculation, and a description of the demographic characteristics of the sample population. The extracted data is in appendix 4.

2.4.2 Study methodology
All the studies included the Harvard Medical Practice Study definition of an adverse event and a two-stage process to capture adverse events. Twenty-one studies employed retrospective review of patient charts.(2, 14-17, 19, 20, 24, 25, 27-34, 37, 43, 44, 48) Two studies compared screening using a trigger tool (traditional retrospective chart review) with prospective screening of frontline staff for adverse events followed by review of patient charts.(22, 125) One study used prospective screening of frontline staff for adverse events followed by chart review.(21) Two studies employed a cross-sectional method for adverse event estimation, i.e. the adverse event rate was a point prevalence with data collected on one day during the hospital admission – reviewing for events in the previous week(125) or 24 hours(13). One of these studies compared three methods: cross-sectional, prospective screening plus chart review and retrospective trigger tool screening plus chart review.(125)

2.4.2.1 Populations studied
The "headline" adverse event rates ranged from under 3%(22, 122) to over 16%(30) (Table 2.2). Of the 25 studies, nine produced national or multi-national adverse event rates,(13-16, 21, 29, 31-33) five produced within-country regional, state or city-based rates,(2, 17, 27, 30, 125) and eleven calculated rates for one hospital or a group of hospitals (Table 2.2).(19, 20, 22-25, 28, 34, 37, 39, 44)
### Table 2.2 Included studies location and headline adverse event rate

<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Location</th>
<th>Headline adverse event rate (confidence interval, CI, or standard deviation, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>New York</td>
<td>3.7% (95% CI 3.2% - 4.2%)</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>Boston</td>
<td>O’Neil 2.7% for HMPS record review, 4.3% for both methods – HMPS record review and reporting/record review (Bates 11%)</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>New South Wales and South Australia</td>
<td>16.6% (95% CI 15.2% - 17.9%)</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>Utah and Colorado</td>
<td>2.9% ± 0.2%</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>London</td>
<td>10.8%</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>Auckland</td>
<td>10.7%</td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>New Zealand</td>
<td>12.9%, incidence 11.2%</td>
</tr>
<tr>
<td>Forster 2004(19)</td>
<td>Ottawa</td>
<td>12.7% (95% CI 10.1% - 16.0%)</td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>Canada</td>
<td>7.5 per 100 hospital admissions</td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>South-western France</td>
<td>Retrospective: 14.5% (95% CI 10.4% - 18.7%), prospective: 15.4% (95% CI 12.2% - 18.7%), cross-sectional: 9.8% (95% CI 6.8% - 12.8%)</td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>Quebec</td>
<td>8.5% (95% CI 7.2-9.8)</td>
</tr>
<tr>
<td>Sari 2007(23)</td>
<td>NHS hospital in England</td>
<td>8.7% (95% CI 7.0% - 10.4%)</td>
</tr>
<tr>
<td>Michel 2007(21)</td>
<td>France</td>
<td>6.6 (95% CI 5.7 – 7.5) per 1000 days of hospitalisation</td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>Aberdeen</td>
<td>7.9% (95% CI 5.6% - 11.2%)</td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>Spain</td>
<td>8.4% (95% CI 7.7% - 9.1%), include pre-hospital events 9.3% (95% CI 8.6% - 10.1%)</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>Sweden</td>
<td>12.3% (95% CI 10.8% - 13.7%)</td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>Rio de Janeiro</td>
<td>7.6% (95% CI 6.0% - 9.2%), incidence density 0.8 (95% CI 0.6 – 0.9) AEs per 100 patient days</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>The Netherlands</td>
<td>5.7% (95% CI 5.1% - 6.4%)</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>Monastir, Tunisia</td>
<td>10% (95% CI 7.6% - 12.3%)</td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>Five Latin American countries</td>
<td>10.5% (95% CI 9.91% - 11.04%)</td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>Eight African countries</td>
<td>8.2%</td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>The Netherlands</td>
<td>4.1% (95% CI 3.3% - 5.1%) in 2004, 6.2% (95% CI 5.0% - 7.6%) in 2008</td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>Lisbon</td>
<td>11.1% (95% CI 9.6% - 12.6%)</td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>Three Dutch cities</td>
<td>Dutch 11% (95% CI 9% - 14%), ethnic minority 10% (95% CI 7% - 12%)</td>
</tr>
</tbody>
</table>
2.4.2.2 Study size

The number of hospitals where patient chart reviews took place ranged from 1(19, 22-24, 34, 44) to 71(21) (Table 2.3). The number of admissions assessed ranged from 450(34) to over 30,000.(2)

Table 2.3 Adverse events studies by number of hospitals studied and patient charts reviewed

<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Number of hospitals</th>
<th>Number of patient charts reviewed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>23</td>
<td>30121</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>1</td>
<td>3141</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>28</td>
<td>14179</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>28</td>
<td>14700</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>2</td>
<td>1014</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>3</td>
<td>1575</td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>13</td>
<td>6579</td>
</tr>
<tr>
<td>Forster 2004(19)</td>
<td>1</td>
<td>502</td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>20</td>
<td>3745</td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>7</td>
<td>778</td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>20</td>
<td>2355</td>
</tr>
<tr>
<td>Sari 2007(23)</td>
<td>1</td>
<td>1006</td>
</tr>
<tr>
<td>Michel 2007(21)</td>
<td>71</td>
<td>8754</td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>1</td>
<td>450</td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>24</td>
<td>5908</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>28</td>
<td>1967</td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>3</td>
<td>1103</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>21</td>
<td>7926</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>1</td>
<td>620</td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>58</td>
<td>11332</td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>26</td>
<td>15548</td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>1</td>
<td>1501</td>
</tr>
<tr>
<td>Sommella 2014(24)</td>
<td>3</td>
<td>1669</td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>20</td>
<td>4023</td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>4</td>
<td>1339</td>
</tr>
</tbody>
</table>
2.4.2.3 Sample populations and exclusion of low risk patients

Ten studies included only adult patients (Table 2.4). (16, 17, 19, 20, 22, 28, 34, 37, 48, 125) Of the remainder that included children, two excluded those aged under one year. (15, 31) Several studies excluded specific patient groups – eight excluded obstetrics; (16, 17, 22, 23, 25, 31, 37, 125) ten excluded short stay (either defined as day cases or admissions with a duration under 24 hours); (14, 15, 20, 23, 24, 29, 32, 33, 37, 43) and a further four excluded these but included deaths within 24 hours. (16, 17, 25, 31) Psychiatry was explicitly excluded by the majority of studies (20 out of 25). (2, 15-17, 19, 21, 22, 24, 25, 27-29, 31-34, 37, 43, 48, 125)

Table 2.4 Adverse events studies by population included

<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Obstetrics</th>
<th>Psychiatry</th>
<th>Paediatrics</th>
<th>Short stay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>✓</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Forster 2004(19)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>✓ deaths included</td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X deaths included</td>
</tr>
<tr>
<td>Sari 2007(23)</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Michel 2007(21)</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>?</td>
<td>?</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>?</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>X deaths included</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>?</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>✓</td>
<td>?</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>?</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Sommella 2014(24)</td>
<td>?</td>
<td>X</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>X</td>
<td>X</td>
<td>✓</td>
<td>X deaths included</td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
### 2.4.2.4 Screening methodology

All studies used a two-stage process to determine adverse events. Three studies included prospective clinician reporting as the screening stage. The retrospective studies all employed a list of clinical triggers to screen for potential adverse events. The percentage of charts triggered ranged from 8% to 62%.

Eighteen of the 25 studies used trigger lists based on the Harvard Medical Practice Study or the adaptation of this by the Quality in Australian Health Care Study. Both of these studies used lists containing 18 trigger criteria but two were different: Harvard included raised temperature (>38.3 degrees Celsius and a length of stay >90th percentile than that expected from the diagnostic group). These were not present on the Australian adapted list which instead included inappropriate discharge home and documentation of dissatisfaction of care or complaint. The Spanish and Latin American studies used the same trigger list, which was based on the Harvard Medical Practice Study but contained 19 triggers and was derived as part of their Adverse Event Identification Project. Vincent and colleagues developed their own lists and these were used by four of the studies.

### 2.4.2.5 Number of physician reviewers

All studies used physician reviewers for adverse event determination. Eight studies used two reviewers in stage two to determine the presence of an adverse event. Of these, one study had investigators (rather than reviewers) examine all adverse events to exclude false positives; one study had two investigators review all adverse events and determine preventability; another study used external experts to review the adverse events which were healthcare-associated infections or involved healthcare products; one developed a consensus methodology to replace the physician second stage and had the nurse screen and determine adverse events in stage one; and another study had one
reviewer only unless it was a difficult case in which a duplicate review was performed. (28) Eleven studies used one reviewer (14-16, 20, 22, 27-29, 32, 43, 125) and in the six remaining the number of stage two reviewers for each chart was not explicitly stated. (13, 21, 25, 34, 37, 48)

2.4.2.6 Extent of chart review
Three studies altered the review period prior to the index admission according to the person’s age – one year if aged less than 65 years and six months if 65 or over. (2,14,27) This corresponded to the trigger of hospitalisation prior to the index admission. Four studies reviewed 12 months prior to the index admission and 12 months after. (16, 17, 31, 33) Two studies had no restrictions on documentation reviewed and hence adverse events could have occurred during any admission prior to the index admission if they were related to the index admission. (30, 32) Not all studies provided this information in their publications.

2.4.2.7 Adverse event eligibility criteria
Most studies described a six-point scale for assessment of causation by healthcare management and/or preventability. As an example, the Australian study (30) six-point scale for causation is given below (the six-point scale for preventability follows the same pattern):

1 = Virtually no evidence for management causation;
2 = Slight-to-modest evidence for management causation;
3 = Management causation not likely, less than 50–50 but close call;
4 = Management causation more likely than not, more than 50–50 but close call;
5 = Moderate/strong evidence for management causation; and
6 = Virtually certain evidence for management causation.
Seven studies did not state their level for causation or preventability or describe a six-point scale. (22, 24, 25, 34, 37, 44, 125) Of the 18 that did provide this information: three used a level of ≥2; (29, 30, 32) fifteen a level of ≥4, to indicate causation by healthcare management and preventability; (2, 13-17, 19-21, 27, 28, 31, 33) and three studies presented adverse event and preventability results at both cut-offs (≥2 and ≥4). (23, 32, 43)
Sixteen studies included events that occurred prior to the index admission but were responsible for, or detected in, the index admission. (2, 14-17, 19, 20, 27, 29-34, 43, 125) Three of these restricted the pre-hospital events to those that occurred at the index hospital (generally during previous admissions, i.e. in-hospital events) (Table 2.5). (15, 16, 21, 25, 31) Three studies did not include events prior to the index admission. (13, 21, 25) Eleven studies included events that occurred in the index admission and were discovered subsequently (15-17, 23, 25, 30-34, 43) five did not include these events, (2, 14, 19, 21, 27) and in the nine remaining it was not stated. Only six studies included all the adverse events (pre, post, in-hospital, out-of-hospital) that were associated with the index admission. (17, 30, 32-34, 43)

Table 2.5 Timing of included adverse events

<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Pre-index in-hospital* events</th>
<th>Pre-index out-of-hospital† events</th>
<th>Detected post-index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>✓</td>
<td>?</td>
<td>X</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Forster 2004(19)</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>✓</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sari 2007(23)</td>
<td>?</td>
<td>?</td>
<td>✓</td>
</tr>
<tr>
<td>Michel 2007(21)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>✓</td>
<td>✓</td>
<td>X</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>✓</td>
<td>✓</td>
<td>?</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>X</td>
<td>X</td>
<td>?</td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>✓</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>✓</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Sommella 2014(24)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>
2.4.2.8 Measurement of adverse event frequency

Studies in which adverse events were associated with more than one admission (e.g. events occurring prior to the index admission but detected in the index admission and those occurring within the index admission which were detected either in that admission or in a subsequent admission) were considered to be reporting a prevalence. In contrast, if events were only able to be related to one admission, the frequency was considered to be an incidence.

Eight studies reported a prevalence of adverse events. (15-17, 30, 31, 33, 34, 43) Two studies calculated both prevalence and incidence. (23, 117) Seven studies reported only an incidence. (2, 13, 14, 19, 21, 25, 27) The remaining eight studies did not provide sufficient description of the timing of their events to establish whether they were quoting incidence or prevalence figures. (20, 22, 24, 28, 29, 37, 44, 125)

Most studies that reported an incidence included only events that were detected in the index admission and none detected subsequently (therefore events occurring prior to the index admission could be included). (2, 13, 14, 19-21, 23, 27, 32) In contrast, one study defined incident events as all events occurring in the index admission (this meant that no pre-index admission events were included but events detected subsequently were eligible). (25)

One study reduced their adverse event rate by 20% to estimate the incident number of adverse events. This corrected for the fact that an adverse event may be related to several admissions. Using this method they corrected their adverse event rate of 16.6% to 13% for the number of adverse events per 100 admissions. (30)
Five studies calculated the incidence density of events as the number of events per 100 or 1000 hospital days. (14, 15, 20, 21, 44) Six studies calculated incidence density per admission. (2, 13, 16, 23, 28, 50) One of these included only adverse events which occurred and were detected in the index admission (and excluded pre-hospital events). (14) Five studies assessed only the event with the greatest impact and did not collect data on the total number of events and therefore were not able to calculate a density of events. (22, 25, 27, 29, 33)

2.4.3 Patient characteristics
An overview of the data extraction regarding patient characteristics and risk of adverse events is shown in Table 2.6 and discussed below.
<table>
<thead>
<tr>
<th>Main results paper (first author, year published)</th>
<th>Gender</th>
<th>Age</th>
<th>Ethnicity</th>
<th>Socio-economic status</th>
<th>Co-morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brennan 1991(2)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>↑ with DRG level</td>
</tr>
<tr>
<td>O’Neil 1993(22)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Wilson 1995(30)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Thomas 2000(27)</td>
<td>↔</td>
<td>↑</td>
<td>↑ (not an independent risk factor after adjustment)</td>
<td>↓ risk preventable AEs if white</td>
<td>ND</td>
</tr>
<tr>
<td>Vincent 2001(28)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Davis 2001(39)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Davis 2002(32)</td>
<td>↔</td>
<td>↑</td>
<td>↑ for Maori, ↑ for Pacific peoples</td>
<td>↔</td>
<td>↑ for musculoskeletal, ↓ for digestive, circulatory</td>
</tr>
<tr>
<td>Forster 2004(19)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Baker 2004(16)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Michel 2004(125)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Bartlett 2008(17)</td>
<td>↔</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>↑ preventable AEs with psychiatric and communicaton problems</td>
</tr>
<tr>
<td>Sari 2007(23)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Michel 2007(21)</td>
<td>↔</td>
<td>↔</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Williams 2008(34)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Aranaz-Andres 2008(14)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>↑ intrinsic risk factors</td>
</tr>
<tr>
<td>Soop 2009(33)</td>
<td>↔</td>
<td>↑</td>
<td>↑ preventable AEs</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Mendes 2009(20)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Zegers 2009(31)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>↑</td>
</tr>
<tr>
<td>Letaief 2010(44)</td>
<td>↔</td>
<td>↔</td>
<td>ND</td>
<td>ND</td>
<td>↔</td>
</tr>
<tr>
<td>Aranaz-Andres 2011(13)</td>
<td>↔</td>
<td>↑</td>
<td>↑ preventable AEs</td>
<td>ND</td>
<td>↑ with intrinsic risk factors</td>
</tr>
<tr>
<td>Wilson 2012(29)</td>
<td>ND</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Baines 2013(15)</td>
<td>↔</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>↑ for digestive, injury/poisoning, genitor-urinary, neoplasm</td>
</tr>
<tr>
<td>Sommella 2014(24)</td>
<td>↔</td>
<td>↔</td>
<td>ND</td>
<td>↔</td>
<td>↔</td>
</tr>
<tr>
<td>Sousa 2014(25)</td>
<td>ND</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>van Rosse 2014(37)</td>
<td>ND</td>
<td>ND</td>
<td>↔</td>
<td>↔</td>
<td>ND</td>
</tr>
</tbody>
</table>
2.4.3.1 Sex

Fifteen studies commented on the relationship of adverse event risk with sex. None of these found a statistically significant relationship between sex and risk of adverse events. (2, 13-17, 21, 24, 26, 28, 30-33, 44, 48)

2.4.3.2 Age

Seventeen studies commented on the relationship of adverse event risk with age. Fourteen of the 17 studies found an increasing risk of adverse events or preventable adverse events at higher age groups and/or with increasing age. (2, 13-16, 27, 29-33, 48) One of these found that patients aged over 65 had a higher incidence of adverse events and preventable adverse events but that after adjusting for patient and hospital characteristics, age was not an independent risk factor. (26) Three did not find a difference in adverse event risk with age. (21, 24, 44)

2.4.3.3 Ethnicity

Three studies commented on the risk of adverse events by ethnicity. A study designed to examine the risk between Dutch patients and ethnic minority patients did not find a statistically significant difference in adverse events risk between the two groups. (37) The New Zealand national study found an increased risk for preventable events in Maori and Pacific compared with non-Maori/Pacific patients. (140) An American study found that fewer white patients suffered preventable adverse events. (74)

2.4.3.4 Socio-economic status

Four studies commented on aspects of socio-economic status, none of which found a statistically significant effect on adverse event risk. An Australian study found a slightly higher adverse event rate for uninsured patients but when this was age adjusted there was no statistically significant effect. (30) The New Zealand national study did not find a difference in adverse event risk by an area-based deprivation index. (139, 140) The Rome hospital study
examined residence (local/other), citizenship, and marital status and did not find any statistically significant differences. The Dutch ethnicity study did not find an effect on adverse event rate with education levels.

2.4.3.5 Co-morbidities

Ten studies reported on the effect of co-morbidities on risk of an adverse event. The relationship with co-morbidity was examined in different ways. Four of these used a measure of co-morbidity called the Charlson Index. The Charlson Index is calculated using the International Classification of Diseases (ICD) codes for the primary and secondary diagnoses. It is a weighted estimate taking into account the number and seriousness of co-morbidities. One study found the risk of surgical adverse events was increased with a score above 4. Another study found a relationship between adverse event risk and preventable adverse event risk with the Charlson Index. The Harvard Medical Practice Study found an increase in adverse event rate with increasing diagnosis related group (DRG) level and this trend was statistically significant. A study examining the risk of preventable adverse events for patients with impaired communication and psychiatric diagnoses found that both conditions were associated with a statistically significant increased risk of preventable adverse events. However when they examined the data using the Charlson Index and adjusted for age, sex, admission and hospital types no significant difference was evident. Another study did not find a relationship between co-morbidity using the Charlson Index and adverse event risk.

Two studies examined co-morbidity using a defined list of intrinsic patient factors (coma, renal failure, diabetes, neoplasia, chronic obstructive pulmonary disease, immunodeficiency, neutropenia, liver cirrhosis, drug addiction, obesity, malnutrition, pressure ulcer, malformations, heart failure, coronary heart disease, hypertension). Both demonstrated an increased risk of adverse events in patients with one or more of these conditions.
factors. One of the studies demonstrated a step-wise increase in risk with each additional factor.\(^{(14)}\) However, another study also looked at intrinsic patient factors and did not find a relationship with risk.\(^{(44)}\)

Two studies analysed co-morbidity according to the patient’s principal diagnosis. One study found the highest adverse event risk for patients with musculoskeletal and digestive conditions and lowest for patients with circulatory, pregnancy/newborn, respiratory diagnoses.\(^{(139)}\) A Dutch study found that, compared to having a circulatory principal diagnosis, patient with diagnoses in the categories of digestive, neoplasm, injury/poisoning, and genitourinary had statistically significant higher risks of adverse events.\(^{(15)}\)

2.4.3.6 Medication
No studies presented relative risk data for the patients’ medication on admission, e.g. risk in patients on anticoagulants compared with patients not on this type of medication.

2.5 Discussion
This systematic review includes a large number of national adverse event studies and updates the de Vries 2008 systematic review for adverse event occurrence. It provides additional information on methodological differences and the relationship of adverse event risk with patient characteristics.\(^{(35)}\)

The systematic review does not include studies employing the Global Trigger Tool or studies that were not available in English. The Global Trigger Tool employs a broader adverse event definition: “unintended physical injury resulting from or contributed to by medical care that requires additional monitoring, treatment or hospitalization, or that results in death”.\(^{(128)}\) This definition includes events that did not result in prolonged hospitalisation and/or disability at discharge – these are pre-requisites in the Harvard
Medical Practice Study definition which is used for this systematic review. Thus the definition of the main outcome is different so the results and patient characteristics cannot be compared between studies and therefore these studies were excluded from the systematic review.

Three large retrospective hospital patient chart review studies that appeared (from the English abstract) to use the same definition and follow the Harvard Medical Practice Study methodology were also excluded. This is because the main paper was written in a non-English language and an English translation could not be obtained. This includes a Danish national study where 176 adverse events were identified in 114 out of 1,097 admissions giving a 9.0% prevalence of admissions with adverse events (40% preventable);(49) a Catalonian study in 4,790 admissions from 15 hospitals identified adverse events at a rate of 7.4%, 43.5% of which were preventable;(146) and a study in five Italian hospitals of 7,573 charts with a 5.2% incidence of adverse events.(147) Whilst these studies may add to the information on incidence, without a detailed description of their methods and patient characteristics, no data was able to be extracted for the systematic review.

2.5.1 Methodological differences
The included studies varied in the population being represented (from single hospitals to national studies), size (number of hospitals included and the number of charts reviewed) and the study sample under review (for example, some studies excluded paediatric and/or obstetric and/or psychiatric and/or short stay patients whereas others included all in-patients of the hospital).

The included studies varied in their application of the chart review methodology. In stage-one the trigger lists differed between studies as did the percentage of charts that were triggered. This will have implications for the number of charts reviewed by physicians for adverse event
determination. A comparison of two of the studies which had a four-fold difference in adverse event rates (3.7% (2) versus 16.6% (30)) found that one study triggered 26% and the other 44%, and at the second stage 17% and 40% were determined to be adverse events. Therefore differences in application of the methodology in both stages contributed to the eventual discrepancy in frequency. (30)

In stage-two there was variation between studies in the use of one or two physician reviewers. If two physicians reviewed a chart in stage two then a third stage was included to adjudicate on disagreement. It is likely that use of additional reviewers/stages will increase the number of events detected. (126)

Studies also varied in terms of the extent of documentation reviewed (some restricted chart review to defined periods on one or both sides of the index admission while others allowed the entire patient chart to be examined). These differences are likely to affect the number of adverse events detected. The Quality in Australian Healthcare Study assessed that 10% of their adverse events were outside of a year from the index admission. (30)

In addition, differences between studies existed in determination of adverse events by level of causality and preventability (≥2 or ≥4 on a six-point scale) and by criteria for eligible adverse events according to event timing and location. Including all events associated with the index admission means that events could have occurred prior to the index admission or have been discovered in subsequent admissions. This will result in a higher number of events and admissions associated with adverse events, than if either the pre-index or post-index events were excluded. This also has implications for reporting on the frequency of disease.
Basic Epidemiology defines prevalence of a disease “as the number of cases in a defined population at a specified point in time” and incidence as “the number of new cases arising in a given period in a specified population”. Studies varied in their ability to report adverse event frequency as incidence or prevalence. Prevalence includes all events associated with admission. This means that events occurring prior to the index admission (but detected in the index admission) and those occurring within the index admission which were detected either in that admission or in a subsequent admission) can be included. In contrast, incidence is the frequency of new cases in admissions. Therefore events may only be related to one admission. Thus either events prior to the index admission or those discovered after the index admission must be excluded from the incidence calculation. Therefore two scenarios are valid: (a) an event may occur in the index admission and be detected during that admission or afterwards; (b) an event may occur either prior to the index admission or during but cannot be detected subsequently. These differences were used to recalculate the Irish National Adverse Events Study figures to enable comparisons to be made with other international studies (Chapters 3 and 4 of this thesis).

Some studies captured the number of events (as well as the number of admissions with events) and therefore were able to calculate an incidence density of events. Others assessed only the event with the greatest impact and did not collect data on the total number of events and were therefore not able to calculate an incidence density or to report on the proportion of admissions with adverse events that suffered more than one event.

2.5.2 Patient characteristics
The majority of the data on patient characteristics was extracted from analyses performed and published in associated papers published after the main results of each adverse events study. Only two patient characteristics and their relationship with adverse events were reported on consistently –
sex and age. Sex did not appear to be related to increased adverse event risk; whereas increasing age was associated with an increase in risk. However, with the increased risk of experiencing an adverse event at higher age groups it is difficult to know whether this represents greater exposure to riskier situations and/or reduced ability to avoid complications. (41) The presence of one or more co-morbidities did appear to be associated with an increased risk of an event. However, the relationship was not assessed using a common method, which made it difficult to compare studies. No studies presented relative risk data for the patients’ medication on admission.
2.6 Conclusion

This systematic review highlighted differences between international adverse event studies in many methodological aspects, including: study population, threshold criteria for causation and preventability, extent of documentation reviewed, number of reviewers per chart and the timing and location criteria for adverse event eligibility. All of these factors need to be taken into account when comparing the results from the Irish National Adverse Events Study with international studies. The information on methodological differences was extracted in order to determine how the Irish National Adverse Events Study results will differ with application of these various international criteria. Apart from age and sex there was very little data presented describing adverse event risk in terms of patient characteristics or risk factors. Results focussed on hospital environment factors such as type of admission, location of adverse event, and responsible department. Sex was not associated with a difference in adverse event risk. Increasing age was associated with increased risk of an adverse event. It is likely that the presence of co-morbidity also increased risk. However, there was scant data on other patient characteristics such as ethnicity, socio-economic status, and medication use.
3 CHAPTER 3 METHODS

3.1 Study Aims and Objectives

3.1.1 Study aims
The primary aim of this thesis was to quantify the frequency and nature of adverse events in acute hospitals in Ireland for the first time using an internationally recognised, retrospective, patient chart review methodology. Secondary aims were to characterise risk by specialty and patient characteristics, establish the rate of preventable adverse events, determine the cost of adverse events, and compare the Irish adverse event rates with incident reporting and those obtained in other international studies.

To do this, the Irish National Adverse Events Study (INAES) was conducted using a random selection of adult in-patient admissions to eight acute Irish public hospitals in 2009.

3.1.2 Study objectives
1. What is the frequency and nature of adverse events for adult patients in major acute hospitals in Ireland?
2. How does the frequency and nature of adverse events for adult patients vary between the medical and surgical specialties in acute hospitals in Ireland?
3. What risk factors are associated with adverse events in major acute hospitals in Ireland?
4. What proportion of adverse events identified by retrospective case note review is also identified by incident reporting?
5. What is the rate of preventable adverse events in Ireland?
6. What is the cost of adverse events to the Irish healthcare system?
7. How does the Irish rate of adverse events compare with other international retrospective chart review studies?
3.2 My role in the Irish National Adverse Events Study

I was involved in the design, implementation and analysis of the Irish National Adverse Events Study. Funding and ethical approval were obtained prior to this MD commencing, as had the random selection of study hospitals. I designed the random selection process for patient admissions, uploaded the electronic admissions data to the study website, developed the protocol, updated the Operations Manual, coordinated the patient chart reviews at each site (including performing reviews of approximately 500 patient charts myself), managed the study database, exported the data into Stata®, “cleaned” the data, analysed the data, drafted the main results paper and delivered an MD thesis. This work was performed with input from the INAES Working Group (which included my thesis supervisors and Professor Conroy who advised on the statistical analysis) and our Canadian research colleagues.

3.3 Study design overview

The Irish National Adverse Events Study was a two-stage, retrospective record review cohort study. The INAES methodology was based on the Canadian Adverse Events Study which employed a modified protocol of the Harvard Medical Practice Study. (2, 16) Similar approaches have been used in other international studies. (14, 20, 22, 23, 25, 27-35, 49, 149) This methodology involves a two-stage review of patient charts (i.e. the records) with nurse reviewers screening charts for “triggers” which may identify an adverse event (stage-one), followed by physician reviewers determining the presence of any adverse event in trigger positive charts (stage-two) (Figure 3.1).
3.4 Adverse event definition

An adverse event was defined as an unintended injury or complication resulting in disability at the time of discharge, prolonged hospital stay, or death and that was caused by healthcare management rather than by the underlying disease process. (2) Disability was restricted to temporary (lasting up to a year) or permanent impairment of physical function. (16) Healthcare management included the actions of individual hospital staff as well as the broader systems and care processes of healthcare, including both acts of omission (failure to diagnose or treat or manage) and acts of commission (incorrect diagnosis or treatment, or poor performance). (16)

3.5 Governance

I managed the day-to-day running of the INAES. A project manager based in the Royal College of Physicians of Ireland was responsible for the budget and reviewer reimbursement. Regular meetings (monthly during study set up and thereafter approximately quarterly) were held with the INAES Working Group. This consisted of the Principal Investigator Professor Williams and Co-Investigators Professors Hickey and Conroy, Drs Condell, O’Connor and Vaughan, and Ms Gillian Walsh (INAES Project Manager).
3.6 Ethical issues
Research ethics approval was obtained from the research ethics committees of the Royal College of Surgeons in Ireland (REC815) and the Royal College of Physicians of Ireland (RCPI RECSAF 04) (Appendices 1 and 2). Each site was offered the ability to obtain additional ethical approval locally or table the existing approvals at their Research Ethics Committees. All opted for the latter.

3.6.1 Informed consent
The Irish National Adverse Events Study was an unlinked, anonymised, national study. Informed consent from individual patients was not required on the basis that patient case notes were irrevocably anonymised at the point of data collection and unlinked from the hospital site. Therefore no adverse event could be traced back to the person who experienced the event or the hospital in which it was experienced. Precedence for identifying national prevalence rates based on collecting unlinked anonymous data in sensitive medical contexts had been established internationally and nationally in conditions such as human immunodeficiency virus infection.(150) In order to avoid inclusion of any current cases, the chart review was retrospective and involved patient notes from four years prior to the study commencing (admissions during 2009). Hospitals were informed that no specific data or results pertaining to their setting could be released back to them as all results would be aggregated.

3.6.2 Data security
Patient chart data was entered by trained nurse and physician reviewers into a password protected web-based data entry tool using the study identification number only. This data was downloaded directly onto a secure server at the Royal College of Surgeons in Ireland. The medical records department of each hospital site held the master list linking the patient details for the randomly selected admissions to the study identification number. Hospital admission data without dates of birth, names or medical record
numbers (MRNs) but including study identification numbers was stored in password-protected sub-folders in the Royal College of Surgeons in Ireland and the Royal College of Physicians of Ireland.

The study database was only accessible to me via a password protected and encrypted computer and laptop. Data for statistical analysis was stored on a password protected sub-folder of an internal drive at the Royal College of Surgeons in Ireland accessible only to the physician researcher and members of the INAES Working Group based at the Royal College of Surgeons in Ireland.

Data from the INAES will be stored electronically for seven years after publication of the main results paper. Following this, it will be destroyed by deletion from the INAES sub-folder and secure destruction of any paper documentation.

In order to maintain confidentiality and protect on-site data security the following strategies were employed:

- Patient names, date of births, medical record numbers, and names of hospital sites were not included in the database.
- The reviewers could not contact individual patients or physicians.
- Unique study numbers were assigned to each study subject to ensure that confidentiality was maintained.
- All data recorded in hardcopy was stored securely in a locked cabinet.
- Charts being abstracted were never left unattended.
- Data was transported to the study database via the study website using secure https secure file format.
- The Royal College of Surgeons in Ireland is equipped with both electronic and physical barriers to prevent any breach of data security.
• The Royal College of Surgeons in Ireland was responsible for converting the data from individual centres into an aggregate database. Results were reported in aggregate format only.
• No identifiable clinical information was transferred by email
• There was no sharing of passwords.

3.6.3 Access to healthcare records

A waiver was granted for the need to seek permission from the Data Controller in each hospital to access the healthcare records as the data was anonymised immediately after initial access.

Only trained nurse and physician reviewers had access to the hospital patient charts. Chart information was required for the study and all information collected was in relation to the admission reviewed and any injury or adverse event recorded therein. Information was collected on site and medical charts were not removed from the hospital. All data was unlinked (from hospital site) and irrevocably anonymised.

If a reviewer had any concerns during the review process about unrecognised potential deliberate harmful acts, illegal acts, or repetitive negligent behaviour, it was permissible to discuss these concerns with the Principal Investigator regarding whether notification of the hospital site of any suspected misconduct was required. However, the chart review was retrospective, involving patient notes from four years prior to the study commencing in 2013, and therefore recent adverse events or issues of misconduct were unlikely to have been included.
3.7 Hospital selection

3.7.1 Hospital inclusion criteria
All acute public hospitals in the Republic of Ireland with a 24-hour emergency department in 2009 were eligible for the study. Public hospitals in Ireland provide approximately 88% of the national acute hospital beds.\(^{(87)}\)

3.7.2 Hospital exclusion criteria
Hospitals with a single clinical specialty focus were excluded.

3.7.3 Hospital sampling frame
Thirty of the 38 hospitals listed in the Irish HSE2012 hospital case mix\(^2\) annual budget adjustment were invited to participate. Eight of the 38 were excluded because they were hospitals with a single clinical specialty focus: i.e. paediatrics, maternity and orthopaedics.\(^{(151)}\)

An invitation letter and opt-in form were posted and emailed to the 30 hospitals (Appendix 5). Hospitals were classified as ‘large’ if total in-patient, day case and emergency department case mix units were over 100,000 per annum and/or the hospital hosted a National Cancer Centre (i.e. where staff with specialist cancer expertise are concentrated\(^{(152)}\)); with the remainder ‘small’. The approximate number of annual case mix units (and distribution into in-patient/day case/emergency units) for the nine large hospitals was 980,000 (22%/37%/41%) and for the 21 small hospitals it was 860,000 (30%/23%/47%).\(^{(153)}\)

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\(^2\) Case mix is an international system which is used to compare activity and costs between hospitals - patient discharge data is classified into groups called DRGs (Diagnosis Related Groups) which are clinically similar and consume similar resources (e.g. appendectomy, hip replacement).
Eighteen hospitals agreed to participate and were randomly sampled. Randomisation was stratified by HSE region (Dublin Mid Leinster, Dublin North East, South and West(154), Figure 3.2) and hospital size. Eight hospitals, one ‘large’ and one ‘small’, from each of the four regions were chosen for the study.

Figure 3.2 HSE regions and local health offices
3.7.4 Hospital site set up
A site initiation meeting was held with each study hospital. These occurred between August and October 2013. The chief executive officer or chief medical officer, clinical leads, and representatives from the hospital’s quality and risk management team, Hospital In-Patient Enquiry (HIPE) Department and Medical Records Department were invited to attend. The background and nature of the study was presented and discussed. Consent was obtained from each hospital site (Appendix 6). Research ethics approval had already been obtained from Royal College of Surgeons in Ireland and Royal College of Physicians of Ireland research ethics committees (Appendix 7). Each site determined whether further ethics approval was required from their local ethics committee. If desired a letter was provided to the hospital for adaptation to inform hospital staff about the study (Appendix 8). Hospitals were offered the opportunity to have one of their own nurses to be trained in the research methodology to undertake the chart reviews at their hospital. If the hospital did not provide a nurse, then an INAES research nurse (employed by the study) performed the stage-one chart reviews at that site.

3.8 Study population (admissions)

3.8.1 Admission inclusion criteria
Admissions of patients aged 18 years or over to an acute public hospital in the Republic of Ireland during 2009 with a hospital stay of 24 hours, or who died within 24 hours of admission, were eligible for inclusion in the study. If a patient had more than one admission, each admission had an equal chance of being selected for the study.

The year 2009 was chosen as it pre-dated the establishment of the National Clinical Care Programmes in Ireland.(100) The purpose of these programmes is to improve and standardise care throughout the health system. Thus, INAES was designed to collect baseline data on adverse events and allow for future studies to assess the effects of these Programmes on relevant patient safety outcomes.
3.8.2 Admission exclusion criteria
In a similar fashion to other international adverse event studies, admissions of patients with a psychiatric or obstetric principal diagnosis were excluded. (16) Obstetric cases were excluded because previous studies have shown a much lower rate of adverse events in this population with its more structured pathway of care. (11, 28, 30, 34) Psychiatric cases were excluded because of the specialist management pathways for these patients, and the study data collection was not designed for these admissions. (139) The requirement for a stay over 24 hours has been used in other studies due to the lower risk of adverse events with very short hospital stays. (16, 34) Admissions that were a transfer from another hospital were also excluded as the likelihood was that full clinical information from the transferring hospital would be unavailable. These exclusions were consistent with the Canadian Adverse Events Study. (16)

3.8.3 Power calculation
A sample size of 1500 admissions was calculated using a 20% rate of adverse events and ±2% precision (with precision improving at lower rates). (30) This allowed a precision of ±5% in any sub-group constituting 20% or more of the total sample. Therefore, at least 187 eligible admissions were required to be reviewed at each hospital.

3.8.4 Admission sampling frame
The sampling frame included all in-patient admissions to study hospitals for patients aged at least 18 years who had a minimum stay in hospital of 24 hours (or died within 24 hours) and excluded admissions with a principal diagnosis related to obstetrics or psychiatry (ICD-10 codes F00-F99 and O29-O927(155)). These codes were mapped into ICD-10 from the Canadian Adverse Events Study which used ICD-9. Early pregnancy (<20 weeks) was included in line with the Canadian Adverse Events Study. (16) Admissions that were recorded in HIPE as being a transfer in from another hospital were also excluded. Note that the hospital stay commenced at the time the patient
entered the hospital and this may have preceded the admission time (i.e. when the patient was formally admitted by the hospital) by several hours, for example, if a person was assessed in the Emergency Department first.

Selection of the study sample of admissions was performed in each participating hospital’s local Hospital In-Patient Enquiry (HIPE) discharge database. HIPE is a health information system which collects demographic, clinical and administrative information on discharges and deaths from acute hospitals in the Republic of Ireland. Discharge diagnoses and procedures are coded using ICD-10 AM/ACHI/ACS 6th edition (International Classification of Diseases, 10th revision Australian Modification Australian Classification Health Interventions/ Australian Coding Standards 6th edition). (156) Data collected on HIPE are shown in the summary page from the HIPE instruction Manual 2009 (Appendix 9). (157) Identifiable HIPE data was unable to be obtained from the central repository at the Healthcare Pricing Office due to the conditions on which such data is collated (i.e. only aggregated anonymised data can be released). Thus, we were advised to obtain this information using the hospitals’ local HIPE databases.

3.9 Hospital In-Patient Enquiry random selection of admissions
A random sample of 300 - 400 admissions for the calendar year 2009 was generated at each site using the hospital’s local HIPE electronic discharge database. These admissions became the index admissions reviewed for the study - i.e. “the episode of care (admission) and hospital stay which is the focus of the chart audit for each case under review”. (158)

I developed the HIPE search strategy and the HIPE search was performed either by me or the local HIPE expert at each hospital site. The HIPE experts were provided with guidance on how to generate the lists (Guidance notes for the HIPE Office and Medical Records Department, Appendix 10) and if they preferred to perform the search themselves they were provided with the
HIPE script, sample screenshots of the process (Appendix 11), and examples of the output in Excel.

The HIPE basic search strategy was as follows: Admission date between 01/01/2009 and 31/12/2009, discharge date 01/01/2009-31/12/2012; In-patient; Patients age in years between 18 and 110; Admission source excludes transfers from other acute hospitals; Principal diagnosis is not between F00 and F99 (i.e. exclude psychiatric); Principal diagnosis is not between O29 and O927 (i.e. exclude obstetric).

3.9.1 Surgery and non-surgery stratification of admissions
In order to maximise the number of adverse events reviewed the sample was stratified such that half of admissions had undergone a surgical procedure (without stratification this figure was approximately one quarter); these admissions were known as the “surgery” group, and the remainder as the “non-surgery” group. This was consistent with the Canadian Adverse Events Study which included 50% of its patients as surgical.(16)

The procedure codes for general anaesthetic, regional and neuroaxial blocks (ACHI 9251400-9251499, 9250800-9251299) were used as a proxy to indicate that surgery was likely to have been performed during the admission. Two HIPE searches were therefore performed - one for admissions with these procedure codes (which were likely to have had a surgical procedure, the “surgery” group) and one for those without the codes (and which were not likely to have had a surgical procedure, the “non-surgery” group) (Guidance notes for the HIPE Office and Medical Records Department, Appendix 10).

The stratification for “surgery” charts was as follows: The All Procedures (ICD-10-AM) is between 9251400 and 9251499 (i.e. general anaesthetic);
The All Procedures (ICD-10-AM) is between 9250800 and 9250899 (i.e. neuroaxial block); The All Procedures (ICD-10-AM) is between 9250900 and 9250999 (i.e. regional block, nerve of head or neck); The All Procedures (ICD-10-AM) is between 9251000 and 9251099 (i.e. regional block, nerve of trunk); The All Procedures (ICD-10-AM) is between 9251100 and 9251199 (i.e. regional block upper limb); The All Procedures (ICD-10-AM) is between 9251200 and 9251299 (i.e. regional block lower limb).

For the “non-surgery” charts the HIPE search requests above were set to ‘is not between’. For example, The All Procedures (ICD-10-AM) is not between 9251400 and 9251499 (i.e. no general anaesthetic).

### 3.9.2 Oversampling

At least 187 eligible admissions were required to be reviewed at each site. Nurses were instructed to review up to a target of 190 - 200 eligible admissions (approximately 100 “surgery” and 100 “non-surgery”) at each site.

Oversampling of admissions at the time of HIPE selection was performed to account for missing charts (estimated to occur in approximately 10% of the sample(16, 43)) and the difficulty of accurately estimating length of stay for admissions of short duration from the HIPE dataset. All in-patient admissions in HIPE start with a length of stay of one day, with no times associated with the admission or discharge dates, thus making it impossible at the time of the HIPE search to exclude patients discharged with a length of stay under 24 hours. Therefore an additional 50 randomly selected admissions were generated for each of the ‘surgery’ group and the ‘non-surgery’ group as part of the HIPE search. This meant that the HIPE selection generated 300 randomly selected admissions for each site.
In two of the hospital sites a second HIPE search and generation of additional randomly selected admissions was later required because the target number of eligible charts was not reached, despite the oversampling. In one site this occurred because gynaecological day cases were inadvertently coded as in-patients in 2009 and in the other site there were a large number of short duration admissions (the hospital stay was under 24 hours). Thus, the INAES nurse reviewer was not able to review sufficient eligible charts from the original list and a second search had to be performed.

Because of the oversample, nurse reviewers were instructed to review patient charts from the first 100 in each of the “surgery” and “non-surgery” lists. Nurses were able to review in any order from that first 100 in each list as the review target for each site was approximately 200 charts (100 each of “surgery” and “non-surgery” eligible charts). The oversample of 50 charts on each list was considered the “back-up” list of patient charts. The nurses were instructed to select charts from the back-up list only when the initial 100 in “surgery” and “non-surgery” had been exhausted. They were also to select these charts in order if possible.

3.9.3 Hospital In-Patient Enquiry sampling process
A screen shot of each stage of the HIPE search was saved to ensure the procedure documented in the Guidance notes for the HIPE Office and Medical Records Department was followed (Appendix 10). The screen shots demonstrated how the full list of admissions for the hospital site in 2009 was narrowed down to the study’s eligible population (i.e. in-patient adults aged at least 18 years, excluding those with an obstetric or psychiatric principal diagnosis according to the provided ICD codes) and then split into the “surgery” and “non-surgery” groups.
The HIPE discharge database contains a random selection function whereby, a percentage of the total search result or a specified number of charts can be randomly selected. The specified number random selection function was used generate the lists of 150 “surgery” and 150 “non-surgery” admissions. Once the two Excel spreadsheets of 150 admissions were generated a column for the study identification number was inserted to the right of the Medical Record Number (MRN) column. Each hospital was allocated a capital letter (e.g. X). The method used to assign the letters was known only to me. Numbers were then added after the letter and underscore, using Excel - X_001 to X_150 for the surgery group and X_151 to X_300 for the non-surgery group. The resulting two Excel spreadsheets became the master lists and were given to the Medical Records Department for chart retrieval.

The local HIPE expert conducting the search removed the patient identifiers of name, date of birth, and MRN. The resulting Excel spreadsheets containing only the study identification numbers and admission data were emailed to me by the HIPE expert. The spreadsheets were saved onto the INAES password protected sub-folders at the Royal College of Surgeons in Ireland and the Royal College of Physicians of Ireland.

I reviewed the spreadsheets and screenshots to ensure the data extraction process had been correctly carried out. Once checked, I manipulated the data into the format required by the MySQL™ INAES database and uploaded it. The format required admission type to be either elective or emergency. Therefore HIPE codes for admission type of 1 (elective) and 2 (elective readmission) were mapped to INAES elective and other HIPE codes (representing emergency, emergency readmission and maternity) were mapped to INAES emergency.(157)
3.10 INAES web-based data collection

3.10.1 Canadian Adverse Events Study

The INAES Working Group made the decision to collaborate with researchers from the Canadian Adverse Events Study (CAES) whilst developing the funding application for INAES to the Health Research Board.(16) The Canadian study was a similarly sized national study among a set of geographically disparate major teaching, large community and small hospitals. The method used in the Canadian study followed the Harvard Medical Practice Study and the Canadian researchers adapted the data collection tools from the UK and Australian studies.(2, 16, 30) The guidance they received from previous researchers saved time in designing their own tools and reduced the likelihood of differences in implementing the Harvard methodology.

Subsequently the Canadian research team have collaborated and shared their research tools with a number of other national adverse event research teams including those from Brazil and The Netherlands. (20, 31) They also developed their data collection tools into a web-based data entry form for the Canadian Paediatric Adverse Events Study.(149) This streamlined the process for collecting chart data and ensured that data could be uploaded to a secure network location. As part of the collaboration with the Canadian researchers, the INAES Working Group secured permission to adapt and utilise this web-based data collection tool (and accompanying Operations Manual) for the Irish study. In addition, this collaboration allowed alignment of the Irish and Canadian methods permitting a comparison between the baseline incidences of adverse events in acute care hospitals between the two countries.
3.10.2 Adaptation of the Canadian data collection tool

The Canadian web-based data entry tool (data collection forms, database and Operations Manual) were modified for the Irish healthcare setting at the time of the reviewer training. This was performed by the Canadian information technology experts and research team, with assistance from me, the INAES Working Group and a technical architect from the Royal College of Surgeons in Ireland (RCSI) information technology department. The hosting database was transferred to RCSI for data collection at the first site. I was responsible for all uploading of hospital HIPE admissions data and management of data entry problems during data collection.

The web-based electronic data collection forms were based on previous paper forms used in other major adverse events studies employing the Harvard Medical Practice Study methodology and contained structured questions to enhance reviewer reliability. The Canadian tool had several other advantages – pre-population of hospital admissions information (dates and diagnoses from each site’s local HIPE discharge database), a streamlined process for recording data (use of compulsory fields and notifications to minimise the amount of missing data), and enhanced data security (data was downloaded on data entry to a secure server without the need for paper-based materials or saving or emailing of electronic forms). It also allowed real-time tracking of the review process at each site, automatic assignment of reliability status, and direct transfer of the whole dataset into a statistical programme for cleaning and analysis. In addition, as part of the collection of the physician review data, the INAES database system automatically determined at the time of data entry which injuries satisfied the study definition of an adverse event (i.e. resulted in disability on discharge, prolonged hospitalisation, or death and was caused by healthcare management). These events then required additional information to be entered.
Members of the INAES Working Group and I adapted the Canadian Operations Manual to produce the INAES Operations Manual. This contained the study protocol and detailed instructions for web-based data collection. I also adapted the Canadian data dictionaries for the INAES dataset. All data collection, definitions and judgement scales used were drawn from the Canadian Adverse Events Study.

3.10.3 Uploading admissions data to the study databases

The INAES web-based data collection tool stored information in five databases – the main study database where data from original chart reviews was stored, three databases for the nurse reliability chart reviews, and one database for the physician reliability chart reviews. Therefore the reliability patient chart reviews were kept separate to the original reviews and did not contribute to the main results analysis (apart from the calculation of the kappa statistic for inter-rater reliability). These databases were in MySQL™ Workbench 6.0. I used the Structured Query Language (SQL) to work with the data.

The web-based data collection required pre-loaded data for it to operate. Study identification numbers and corresponding admissions data from HIPE were pre-populated and matched to the patient chart under review. To enable this, the HIPE search data was formatted and uploaded into the MySQL™ study database. Each hospital's HIPE output was different in terms of use of capitals in column headings, date format, formatting of number cells and these needed to be made consistent with the database requirements.

The following columns were uploaded in a standard format – hospital identifier (a number corresponding to the allocated letter), study identification number, age at admission, gender, chart status, admission type (emergency or elective), date of admission (MM/DD/YYYY), date of discharge (MM/DD/YYYY), principal diagnosis, additional diagnoses, procedures
performed. Only one row was uploaded for each admission. An insert statement in SQL was used to generate each line of data to be uploaded from the Excel spreadsheet and this was copied into the MySQL™ database.

Uploaded admissions data had the chart status set to ‘0’. This meant that the patient chart could be seen on the nurse reviewer (stage-one) drop down list of patient charts to be reviewed at each site. Once the patient chart was reviewed and submitted, the status changed to ‘2’ if it was not triggered indicating review of this chart was complete. If the chart was triggered, the status became ‘1’ and the chart was now seen on the physician reviewer (stage-two) list of charts to be reviewed at each site. When a physician finished their review and submitted it, the status went to ‘2’ also.

I provided the “helpdesk service” for technical problems in the field and was able to refer to contacts in the RCSI Information Technology Department and Canadian Institute for Health Information for additional support, where required.

3.11 Reviewer selection and training

In order to enhance accurate detection and judgement of adverse events, recruitment of reviewers required minimum clinical and patient safety/audit experience criteria standards to be met. These are described below.

3.11.1 Reviewer selection

Nurse reviewers were recruited via advertisements circulated on the recruitment websites of the Royal College of Surgeons in Ireland and the Royal College of Physicians of Ireland and the Irish Research Nurses Network. Nurses were required to be registered General Nurses with the Nursing and Midwifery Board of Ireland with a minimum of 7 – 10 years clinical experience. A good understanding of patient safety and risk
management, demonstrable appreciation of ethical considerations relating to patient safety and a broad understanding of research methodology were considered essential. Hospital sites were offered the ability to provide their own local nurses (subject to the aforementioned criteria). This was considered an advantage for the site in terms of enhancing local staff capacity through receipt of training in the methodology enabling the ability to conduct local chart review studies in the future.

Seven nurse reviewers were trained (four local nurses), six of whom reviewed patient charts for the study. One local nurse was unable to contribute reviews due to her workload increasing at the time of the review. Each nurse had a minimum of 7 years nursing experience and all had additional experience in clinical research, audit, hospital management, and/or education. Two of the study nurses had been involved in a previous patient chart review study of surgical mortality in Irish hospitals.(159)

I was recruited via advertisement in the Royal College of Surgeons in Ireland network. A minimum of three years clinical experience, a post graduate training College membership or fellowship, and an understanding of patient safety, risk management and human factors were all required for the post of clinical research fellow. Two recently retired (within the preceding three years) physicians were recruited through advertisements circulated on the recruitment websites of the Royal College of Surgeons in Ireland and the Royal College of Physicians of Ireland and an email sent to retired physicians. Experienced physicians with a sound practical understanding and appreciation of the Irish Health System and an interest in improving patient safety and minimising adverse events were sought. All reviewers were required to demonstrate an appreciation of the ethical considerations relating to patient safety.
All three physician reviewers were specialists – two retired respiratory physicians and I am a public health medicine physician. The retired physicians had experience with review of practitioner performance issues, audit and teaching, and I had skills in the assessment of reports of adverse drug reactions and medical device incidents.

### 3.11.2 Reviewer training

The training course on the review methodology was delivered to all ten reviewers (nurses and physicians) at the same time to ensure standardisation and enhance inter-rater reliability. This occurred in October 2013. Researchers from the Canadian Adverse Events Study and the Canadian Paediatric Adverse Events Study conducted the face-to-face training over 2½ days prior to the commencement of the study. (16, 149)

The training included presentations by the Principal Investigators of the Canadian and Irish Studies (Professors Baker and Williams) detailing the background to adverse event studies and plans for the Irish study plus additional presentations on trigger tools, Irish healthcare data in HIPE and reliability monitoring. The Operations Manual for the Canadian study had been adapted for the Irish study and reviewers were all given bound copies to refer to during the training and onsite visits.

The group reviewed an anonymised patient chart together covering both stages of the patient chart review process. The web-based data collection tool was demonstrated variable by variable. The group was split into physician and nurse reviewers to review five additional anonymised patient charts. These were bound hardcopy charts from Canadian patients to simulate real hospital charts. They were reviewed by each reviewer independently and then entered into the training website. They were then discussed in the nurse or physician groups.
3.11.2.1 Training inter-rater reliability

Reviewers independently reviewed 20 standard reliability charts immediately following the training course and prior to going into the field. These were electronic, scanned and anonymised Canadian patient charts. Two of the Canadian collaborators (one nurse and one physician) also performed the nurse or physician reviews. Reviewers had two weeks to complete the reviews and data was entered into the training website. The results were collated and assessed for inter-rater reliability by calculating the kappa statistic. This examined observer agreement between the nurses for potential adverse event determination (i.e. was the chart triggered or not) and between the physicians for adverse event determination.

The overall kappa result for all the nurse reviewers and the Canadian nurse reviewer was 0.30 (95% CI 0.19 – 0.43). The low kappa for the nurses was due to a subset of the nurses being over sensitive and triggering nearly all of the charts. The kappa results for all the physicians and the physician reviewer were 0.38 (95% CI 0.15 – 0.69) for injury identification and 0.24 (95% CI 0.08 – 0.42) for adverse event determination. The low kappa for the physicians was due to one physician determining fewer injuries and therefore fewer adverse events.

The training charts data and kappa results were discussed in the nurse and physician reviewer groups, including the Canadian collaborators, via two WebEx™ online meeting teleconferences. Each reviewer received feedback on the overall chart review adverse event findings, their performance and the kappa statistic results.

To further enhance inter-rater reliability, each individual nurse had support on their initial ten study charts by one of the INAES study investigators who was
also a nurse reviewer and had performed well on the training charts. All reviewers were encouraged to discuss difficult cases with other reviewers at the site (as long as the chart was not assigned as reliability). Physician reviewers tried to overlap with each other at each site.

3.11.2.2 On-site inter-rater reliability testing
I assigned 10% of the charts for reliability double review using an SQL instruction which allocated reliability status to one in ten patient charts in the database. These charts were also uploaded into the nurse reliability databases. This ensured that the reliability review could be entered but would not overwrite the original chart review data. Reliability status for physician charts was assigned to nurse reliability charts that were triggered. If additional physician reliability charts were required to obtain a target of 10% of physician charts per site, then this was allocated to the closest triggered chart to an un-triggered nurse reliability chart.

In this way approximately 10% of the patient charts were re-reviewed by all nurse or physician reviewers at each site. The kappa statistics in the field improved to: nurses 0.78 (95% CI 0.69-0.88) and physicians 0.59 (95% CI 0.37-0.79).

3.12 Data collection
Data collection commenced at the first site in December 2013. No reviewers were able to work in the field until the study team were satisfied with the training and reliability results for the nurse and physician reviewers. Prior to data collection, the main review nurse at each site and I liaised with the Medical Records Department regarding chart retrieval timeframes and organising a room to conduct the reviews. This room needed to have internet access, desk space for two reviewers and the ability to shelve approximately 200 patient charts. It also needed to be secure with access restricted to reviewers and Medical Records staff. Medical Records assigned the charts
as “out” to this room. In some hospitals laboratory and radiology results and other elements of the patient chart were on a hospital electronic system and access to this (including training) was organised for reviewers for the duration of the review period. Key contact people (medical records, laboratory, radiology) were nominated for the reviewers. Access cards and hospital identification badges were also arranged for reviewers for the duration of the review period at the site. Reviewers signed confidentiality agreements regarding access to healthcare records according to local policy.

3.12.1 Demographic and administrative data collection
Demographic and administrative data on the index admissions (age, sex, admission and discharge dates, discharge diagnoses and procedures and diagnosis related groups, discharge consultant specialty code, admission type, medical card status, length of stay) were collected at the time of random selection from the HIPE database at each site.

National demographic data for adult in-patients in acute public hospitals during 2009 was provided by the Healthcare Pricing Office and generated using the same HIPE search strategy as for the INAES admission sampling (see Guidance notes for the HIPE Office and Medical Records Department, Appendix 10).

3.12.2 Patient chart data
Nurse and physician reviewers used laptops to enter study data directly into the secure INAES study website. Reviewers accessed the internet on their laptops through a mobile broadband stick inserted into the laptop or a password protected mobile Wi-Fi device. Paper forms were provided to all reviewers to use if electronic data entry was not possible. If this occurred, the reviewer entered the data into the website as soon as practically possible.
The stage-one and stage-two patient chart reviews centred on the index admission and all documentation 12 months prior to the admission and 12 months after discharge. Reviewers were instructed in the Operations Manual to include triggers or adverse events that:

1. Are a consequence of healthcare management prior to the index hospitalisation and were discovered during the index hospitalisation, or;

2. Occurred during the index hospitalisation and were discovered during the index hospitalisation, or;

3. Occurred during the index hospitalisation but were discovered in a subsequent hospitalisation.

This was displayed in the Operations Manual with adverse events eligible for inclusion as types 1-3 and ineligible events as types 4-6 in grey (Figure 3.3).

<table>
<thead>
<tr>
<th>Event</th>
<th>Prior to Index Admission</th>
<th>Index Admission</th>
<th>Subsequent to Index Admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>O -----→ D</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>O</td>
<td>D</td>
</tr>
<tr>
<td>3</td>
<td>O ----------------→ D</td>
<td></td>
<td>D</td>
</tr>
<tr>
<td>4</td>
<td>O -----→ D</td>
<td></td>
<td>D</td>
</tr>
<tr>
<td>5</td>
<td>O ----------------→ D</td>
<td></td>
<td>D</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td>O -----→ D</td>
</tr>
</tbody>
</table>

O = occurrence of AE  D = detection of AE

Figure 3.3 Timing of healthcare management and the adverse event

There was no limit on the amount of time a physician or nurse reviewer could spend reviewing a patient chart.

3.12.3 Nurse reviewer eligibility check

Nurse reviewers conducted an eligibility check of the index admission prior to commencing review of each patient chart to exclude patients who had a hospital stay of less than 24 hours (and were discharged). The date of admission was the date of registering the person as an in-patient in HIPE.
and not necessarily the length of hospital stay. This duration was estimated manually through review of the admission documentation in the patient chart to determine the approximate times and dates the patient entered and left the hospital.

In addition, nurse reviewers excluded obstetric admissions that were uncomplicated births and were missed by the principal diagnosis ICD-10 exclusion criteria. This occurred if the principal diagnosis was coded as non-obstetric. This provided a second eligibility screen.

### 3.12.4 Stage-one patient chart review

#### 3.12.4.1 Overview

Stage-one involved nurse reviewers screening for potential adverse events using a list of 18 clinical scenarios called ‘triggers’ (e.g. unplanned readmission, hospital acquired infection, adverse drug reaction) which may indicate the presence of a potential adverse event. This list was the same as the Canadian Adverse Events Study, and similar to the original Harvard Medical Practice Study. (2, 16, 30)

Data on co-morbid conditions was also collected by nurse reviewers. All data was entered using the web-based data entry tool. One nurse reviewed each chart. Ten percent of the charts were flagged as reliability charts - a red box appeared on the data entry screen on submission of the original chart review by the nurse. These charts were then set aside to be re-reviewed by all the nurse reviewers at that site.
3.12.4.2 **Review start**

After selecting a patient chart for review the nurse reviewer found the matching study identification number (study ID) on the master list. The reviewer entered the study ID and date of admission onto the sign-off sheet and proceeded to review the chart.

3.12.4.3 **Stage-one demographic and hospital stay data**

The pre-loaded patient demographics (age, sex, dates of admission and discharge, admission status as elective or emergency, discharge diagnoses and procedures) were checked by the nurse reviewer to ensure they were working on the correct chart. The HIPE-extracted principal discharge diagnosis, additional diagnoses and procedures were pre-populated as ICD-10 codes and accompanying textual descriptions. The nurse reviewers entered a brief description of the admitting diagnosis at the time of admission (this may have differed significantly from the discharge diagnosis) and the main diagnosis on discharge. The nurse reviewer also entered the patient’s discharge status as “alive” (if they were discharged alive) or “dead” (if they died during the index admission). The location to which the patient was discharged, or transferred to, was indicated from a drop-down list (acute care, rehabilitation, long-term care, home, etc.).

The nurse reviewers wrote a synopsis of the patient’s hospital stay during the index admission and relevant admissions before or after the index admission. The reviewers then commented on whether the documentation in the chart for the index admission was sufficient to determine the presence or absence of a trigger for a potential adverse event. If the reviewer indicated it was insufficient, they were required to document which sections were deficient (e.g. admission history and physical, discharge summary, etc.). In the event that certain sections necessary to complete the review, were judged by the reviewer to be missing, the reviewer rated the documentation as inadequate. For example, this would be the case if the report from a computerised tomography (CT) scan was missing that was critical to the
determination of the presence or absence of a trigger. These charts were excluded and the chart review stopped. A new chart review was then commenced. If the outcome of the trigger assessment was not likely to be altered by missing or inadequate documentation then data entry continued.

3.12.4.4 Stage-one co-morbidity data

The nurse reviewer conducted a detailed assessment of co-morbidity. This was defined as conditions diagnosed prior to the index admission and present prior to, or at the time of, the index admission. The reviewer was required to answer “yes” if a particular condition was documented in the notes and “no” if there was documentation that the co-morbid illness was not present. Evidence from a medication list alone was not considered sufficient to support the presence of a particular co-morbid illness.

Each illness was defined and the relevant sections of the chart to be examined were outlined in the Operations Manual in order to confirm the diagnosis. For most illnesses nurses were instructed to look at physician documentation only. Exceptions to this were hypertension, asthma, diabetes, stroke, dementia when other sections such as radiology reports and nurse clinics could be included. Data was collected on the following groups of co-morbid illness. These groupings were based on those in the Canadian Operations Manual.

- Cardiac and vascular (coronary artery disease, cardiomyopathy, congestive heart failure, deep vein thrombosis, hypertension, peripheral vascular disease, previous myocardial infarction, valvular heart disease, other cardiac/vascular disorder)
- Respiratory (asthma, severe chronic obstructive pulmonary disease, other respiratory disorder)
- Gastro-intestinal (liver disease, cirrhosis, peptic ulcer disease, other gastro-intestinal or liver disorder)
• Endocrine (diabetes, secondary end organ damage, dyslipidaemia, other endocrine disorder)
• Neurological (acute confusional state, dementia, Parkinson’s, stroke/TIA, other cerebrovascular neurological disorder)
• Renal (renal failure, renal dialysis, other renal disorder)
• Haematologic (chronic anaemia, other haematological disorder)
• Cancer (metastatic, leukaemia, lymphoma, non-metastatic, other cancer)
• Bone/joint disorders (connective tissue disease, osteo/rheumatoid arthritis, other bone/joint disorder)
• Disability (blind, deaf, hemiplegia, wheelchair bound, other disability)
• Psychiatric (depression, schizophrenia, other psychiatric disorder)
• Psychosocial (alcoholism, smoking status, drug abuse, homeless, other psychosocial disorder)
• Infection (human immunodeficiency virus /AIDS, other infection)
• Trauma (multiple traumas, other traumas)
• Nutritional status (cachectic, obese, other nutritional disorder)
• Other co-morbidity, do not resuscitate status, part of an experimental protocol

3.12.4.5 Stage-one trigger data
The next part of the data collection form was a review of the 18 triggers screening for potential adverse events (Table 3.1). The nurse reviewer entered “yes” or “no” against each trigger. A “yes” response indicated that the review had identified evidence in the patient chart in support of the trigger. A “no” response indicated the reviewer found no such evidence. For each trigger identified, the nurse reviewer entered the date the trigger scenario occurred or was first noticed, and filled in text fields with the description of its cause, nature, outcome, treatment and any other clinical details relevant to the trigger scenario.
Table 3.1 List of triggers used by stage-one nurse reviewers

<table>
<thead>
<tr>
<th>Trigger number</th>
<th>Trigger description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Unplanned admission (including readmission) as a result of any healthcare management within the 12 months prior to the index admission</td>
</tr>
<tr>
<td>2</td>
<td>Unplanned admission to any hospital within the 12 months after discharge from index admission</td>
</tr>
<tr>
<td>3</td>
<td>Hospital-incurred patient injury (including any harm, injury or trauma occurring during the index hospital stay)</td>
</tr>
<tr>
<td>4</td>
<td>Adverse drug reaction</td>
</tr>
<tr>
<td>5</td>
<td>Unplanned transfer from general care to intensive care</td>
</tr>
<tr>
<td>6</td>
<td>Unplanned transfer to another acute care hospital (excluding transfers for tests, procedures, or specialised care not available at referring hospital)</td>
</tr>
<tr>
<td>7</td>
<td>Unplanned return to the operating theatre</td>
</tr>
<tr>
<td>8</td>
<td>Unplanned removal, injury or repair of organ during surgery, invasive procedure or vaginal delivery</td>
</tr>
<tr>
<td>9</td>
<td>Other patient complication e.g. acute myocardial infarction, stroke, pulmonary embolism, etc. (includes any unexpected complication that is not a natural progression of disease or an expected outcome of treatment)</td>
</tr>
<tr>
<td>10</td>
<td>Development of neurological deficit not present on admission but present at the time of discharge from the index hospital stay (includes neurological deficits related to procedures, treatments or investigations)</td>
</tr>
<tr>
<td>11</td>
<td>Unexpected death</td>
</tr>
<tr>
<td>12</td>
<td>Inappropriate discharge to home/ inadequate discharge plan for index admission (excluding “against medical advice”)</td>
</tr>
<tr>
<td>13</td>
<td>Cardiac or respiratory arrest (successful)</td>
</tr>
<tr>
<td>14</td>
<td>Injury related to abortion or labour and delivery</td>
</tr>
<tr>
<td>15</td>
<td>Hospital-acquired infection or sepsis (excluding infections/sepsis occurring less than 72 hours after admission)</td>
</tr>
<tr>
<td>16</td>
<td>Dissatisfaction with care documented in the medical record and/or evidence of complaint lodged (including documented complaint, conflict between patient/family and staff, discharged against medical advice)</td>
</tr>
<tr>
<td>17</td>
<td>Documentation or correspondence indicating litigation, either contemplated or actual</td>
</tr>
<tr>
<td>18</td>
<td>Any other undesirable outcome not covered above</td>
</tr>
</tbody>
</table>
All charts identifying at least one trigger were forwarded for stage-two physician review of “triggered charts”. Charts without any triggers were not further reviewed unless they were highlighted as a reliability chart.

Trigger number 14 (Injury related to abortion or labour and delivery) was included in line with the Canadian Adverse Events Study which also excluded patients with obstetric principal diagnosis. This is because although most obstetric cases would have been excluded from the sample, an injury related to a termination of pregnancy or a delivery requiring admission to an acute public hospital may have been included.

Detailed information from the INAES Operations Manual about each trigger is included in Appendix 12.

3.12.4.6 Nurse reviewer potential adverse event determination

If any of the 18 triggers were indicated as present by the nurse reviewer, the presence of a potential adverse event (i.e. a trigger) was then automatically indicated on the data entry screen at the end of the trigger assessment screens. In this case, the nurse reviewer was asked to indicate the maximum harm category incurred by the patient as a result of healthcare management delivered either prior to, or during, the index hospitalisation. Harm was defined as the “temporary or permanent impairment of physical or psychological body function or structure”.(158)

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) categorisation was used to classify the overall impact of all the potential adverse event.(161) Categories E to I were included (Table 3.2). This categorisation was designed for medication error; however, it was used for classification of overall patient harm in the Canadian adverse event studies.(16, 149) The NCC MERP categories A to
D, which include “no error” and “error without harm”, were replaced by the option “No evidence of harm”.

### Table 3.2 Nurse reviewer categorisation of the maximum impact of the adverse event

<table>
<thead>
<tr>
<th>NCC MERP Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>Contributed to or resulted in temporary harm to the patient and required intervention</td>
</tr>
<tr>
<td>F</td>
<td>Contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalisation</td>
</tr>
<tr>
<td>G</td>
<td>Contributed to or resulted in permanent patient harm</td>
</tr>
<tr>
<td>H</td>
<td>Required intervention to sustain life</td>
</tr>
<tr>
<td>I</td>
<td>Contributed to the patient’s death</td>
</tr>
</tbody>
</table>

Nurse reviewers were also asked if an adverse event had occurred using the definition: “The patient sustained (1) an unintended injury (2) resulting in death, temporary or permanent disability and/or prolonged length of stay as a (3) consequence of health care management?” (158) Nurse reviewers documented the number of adverse events. It is important to note that the presence of a potential adverse event (a trigger) did not necessarily indicate the nurse reviewer found an adverse event. Hence it was possible for nurse reviewers to trigger a chart and indicate that no adverse event had occurred. For example, if the patient had an allergic reaction to a medication that did not result in disability at discharge, prolonged hospitalisation or death.

This concluded the stage-one review.
3.12.5 Stage-two physician chart review

3.12.5.1 Overview
Stage-two of the patient chart review involved physician review of triggered charts to determine whether an adverse event had occurred. Physicians reviewed the patient chart, triggered by the nurse review, to identify adverse events which occurred within 12 months before, or during, the index admission and were detected either during the index admission, or within 12 months following discharge.

First, the presence of any unintended injuries was identified. An unintended injury was defined as “all additional morbidity resulting from complications in healthcare management”.(158) Each injury was analysed in a structured manner via the INAES study website to determine whether or not it satisfied the definition of an adverse event. This determination was a built-in feature of the web-based data collection tool. All suspected injuries which may be adverse events were entered and the physician reviewer was required to answer a series of questions to determine whether each one satisfied the following definition:

“An adverse event must fulfil all three criteria

(a) Unintended injury

(b) Disability at discharge or prolonged hospital stay or subsequent hospitalisation or death

(c) Caused by healthcare management”(158)

Injuries were classified according to their association with death, disability at discharge, prolongation of hospital stay, subsequent hospital admission, interventions and out-patient visits. The physician determined the extent to which healthcare management, rather than the patient’s disease process, was responsible for the injury. The physicians used their professional judgment to estimate the number of additional hospital days directly attributable to adverse events and judged the preventability of each event. A
consultant surgeon was available for advice on surgical cases, if required. There were two physician reviewers working at each site and discussion of difficult cases was encouraged (if the chart was not a reliability chart, whereby reviews had to be independent). Each triggered chart was reviewed by only one physician. A 10% sample of these charts was independently reviewed by the other physician on site for assessment of inter-rater reliability.

3.12.5.2 Clinical information
Physicians logged onto the study website and selected the study identification number corresponding to the patient chart under review. They had to enter the correct admission date before they were able to view the pre-populated HIPE information and the nurse reviewer documentation of diagnoses, discharge status/destination, clinical summary and list of positive triggers. These were used both as a guide and for confirmation that the reviewer was working on the correct chart. Physician reviewers were asked to provide a brief clinical summary of the index admission and any relevant injuries or complications.

3.12.5.3 Unintended injury
The physician reviewers identified the presence of any “suspected injuries” requiring adverse event determination, i.e. where the patient sustained an injury or near miss that was unintended or unexpected. An unintended injury was defined as “all additional morbidity resulting from complications in healthcare management”.(158) Injuries not caused by healthcare management, e.g. traumatic injury leading to hospitalisation, were excluded.(158) The physician reviewer was first asked whether the patient experienced an injury. The reviewer was able to answer “yes”, “no”, or “near miss”. If the reviewer indicated “yes” or “almost injured”, they entered a brief description of each suspected injury or near miss into the website.
The INAES Operations Manual defined a near miss as “an event which, if left uncorrected, may have developed into an unintended injury, resulting in temporary or permanent disability, including increased length of stay and financial loss caused by clinical care rather than disease process”. (158) An example of a near miss given in the Operations Manual was: a patient on digoxin who did not have a digoxin level checked until day four when it was found to be high, digoxin was discontinued and no symptoms of toxicity were noted.

If an episode contained multiple injuries reviewers were advised to enter linked injuries under one description. For example, an event that involved nausea, vomiting and dehydration, was entered and analysed as one injury, rather than three. If the patient developed a wound infection two days later which was not linked to the previous injury, then the wound infection would be entered and assessed as a separate injury. There was no limit to the number of injuries a physician reviewer could enter for each admission.

The physician entered a description of the clinical context surrounding the injury or near miss and then proceeded to the “Disability” and “Causation” sections for automatic adverse event determination.
3.12.5.4 Disability

Disability was defined as “temporary or permanent impairment of physical function (including disfigurement), or mental function or economic loss even in the absence of such impairment”.(158)

The impact of the injury on healthcare services was assessed. The physician reviewer was asked to indicate whether the injury or complication resulted in:

- death
- prolonged hospital stay (the patient’s length of stay exceeded the expected length of stay for management of the admission diagnosis)
- disability at discharge (includes disability of any degree of severity that was not present on admission)
- subsequent hospital admission (the patient was readmitted to hospital for further management of the injury/complication, not including visits to the Emergency Department)
- intervention or treatment without sequelae listed above (the patient received treatment or an intervention but the length of stay was unchanged, there was no disability, readmission, or death)
- out-patient visits (the patient underwent extended and repeated follow-up visits in an out-patient clinic for direct management of the injury/complication)
- none of the above.

The reviewer was able to select all that applied. They then provided a description of its impact on the patient. Injuries that were not associated with at least one of the top four options (death, prolonged hospital stay, disability at discharge, or subsequent hospital admission) did not meet the criteria for an adverse event. In this latter case the injury might still qualify as a near miss and the assessment proceeded to the “Causation” section.
If the injury was associated with death, prolonged hospital stay, disability at discharge, or subsequent hospital admission then the physician reviewer proceeded to enter more information. The physician reviewer was asked to provide an estimate of the portion of the entire hospitalisation that was due to the adverse event – as “none”, “some” or “all” - to determine the number of days that were attributable to the event. This was calculated based on the variance from the expected length of stay and physicians were advised that calculation should err on the side of the smaller estimate in a range. For example, if a patient with an uncomplicated shunt repair developed pneumonia on day 3, was treated with intravenous antibiotics, and was discharged on oral antibiotics on day 7; some of the hospital stay would have been attributable to the adverse event. The estimated length of stay for shunt repair is 4-5 days, the actual stay was 7 days and therefore the stay attributable to the adverse event is 2 days. Only a whole number was permitted to be entered. Attributable days included days in the index hospitalisation and readmissions. The estimation of expected length of stay was based on any documentation in the chart indicating this or the physician’s judgement of the disease progress during the admission.

Physician reviewers then judged the degree of physical impairment attributable to the event on the day of discharge from the list below:

- No physical impairment or disability
- Minimal impairment and/or recovery in one month
- Moderate impairment, recovery in one to six months
- Moderate impairment, recovery in six months to one year
- Permanent impairment, disability 1-50%
- Permanent impairment, disability > 50%
- Death
- Unable to determine
Permanent disability was defined as lasting greater than a year. (16, 30) Physician reviewers were advised that grading a disability as greater or less than 50% required consideration of the patient's potential for work and activities of daily living. To assist reviewers in this grading they were provided with the following definitions of disability severity (158):

“Mild”: the patient can perform basic life management functions and can use mainstream methods of transportation and communication. The patient is able to independently perform most activities of daily living but may require some intermittent assistance.

“Moderate”: the patient is able to perform some activities of daily living but may require assistance with dressing, toileting, and walking i.e. at least four hours of assistance per day.

“Severe”: significant disability which impairs age appropriate performance of daily activities and may be related to neuromotor, auditory, communication, visual, cognitive function or other physical disability.

3.12.5.5 Causation

The physician reviewer was required to indicate whether, in his/her opinion, there was evidence in the medical record that healthcare management caused the patient’s injury. The process involved answering a structured series of questions to assist the physician reviewer in reaching a decision:

- Is there a note in the medical record indicating that healthcare management caused the injury?
- Is there a note in the medical record suggesting the possibility of an injury from the patient’s disease?
- Does the timing of the events suggest that the injury was related to the treatment or diagnostic procedure?
- Does the timing of the events suggest that the injury was related to the lack of treatment?
- Are there other reasonable explanations for the cause of the injury?
- Was there an opportunity prior to the occurrence of the injury for intervention which might have prevented it?
- Is lack of treatment or delayed treatment a recognised cause of this injury?
- Is lack of diagnosis or delayed diagnosis a recognised cause of this injury?
- Is the treatment given to the patient a recognised cause of this injury?
- Is this injury a recognised complication of the patient underlying disease?
- Was the injury recognised during the index admission?
  - If “yes”, was the appropriate action taken?
  - Did the injury respond to the appropriate action?

The assessment of causation concluded with the statement “After due consideration of the clinical details of the patient’s management, irrespective of preventability, and your response to the questions above – what level of confidence do you have that the healthcare management cause the injury?” The following options were provided on a six-point scale:

1. Virtually no evidence of management causation
2. Slight to modest evidence of management causation
3. Management causation not likely (less than 50/50, but “close call”)
4. Management causation more likely (more than 50/50, but “close call”)
5. Moderate to strong evidence of management causation
6. Virtually certain evidence of management causation

Physician reviewers were aware that the event would only be recorded as an adverse event if causation was coded as one of the last three options (i.e. at a level of four or greater). 126
3.12.5.6 Adverse event location and specialty

If the injury qualified as an adverse event, the data entry screens proceeded to information about the location and timing of the event and under which healthcare specialty. The location was broken down into inside or outside the index hospital and, within these groups, into more specific locations. Inside locations were a list of options including the patient’s ward, operating theatre, recovery room, therapy/rehabilitation, pathology, service area, procedure room, radiology, intensive care, emergency department, hospital bathroom, in-patient clinic, out-patient clinic, The options provided for outside hospital were ambulatory care unit, physician’s office (e.g. general practitioner), home, community hospital, and other. 

Physician reviewers were then asked to indicate the timing of the event – when it occurred and when it was detected – in relation to the index event. Only events that occurred prior to the index admission and were detected in the index admission, or occurred in the index admission (these could have been detected in the index admission or a subsequent admission) were included as adverse events to be analysed. This is depicted in Table 3.3 below:

Table 3.3 Timing of healthcare management and the adverse event (AE)

<table>
<thead>
<tr>
<th>Prior to index admission</th>
<th>Index admission</th>
<th>After index admission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O—&gt;D</td>
<td></td>
</tr>
<tr>
<td></td>
<td>O—&gt;D</td>
<td></td>
</tr>
<tr>
<td></td>
<td>O—&gt;D</td>
<td></td>
</tr>
</tbody>
</table>

O = occurrence of AE  D = detection of AE
Physician reviewers next identified the most responsible service at the time of the adverse event, i.e. which service was responsible for the majority of care delivered at the time the adverse event occurred. Initial options were the emergency department, intensive care unit, surgical service, medical service, and other. Further drop down lists were provided for all options other than the emergency department to enlist the sub-specialty. Note “other” included departments such as audiology, pharmacy, podiatry, etc.

3.12.5.7 **Adverse event classification**

Adverse events were classified into ten categories, listed below. The physician reviewer was able to select all the categories which applied to the adverse event being reviewed. This was completed for adverse events only.

1. Diagnostic event
2. Surgical-related event
3. Fracture-related event
4. Anaesthesia-related event
5. Obstetric-related event
6. Medical procedure-related event.
7. Drug-related event
8. Fluid-related event
9. Therapeutic adverse event
10. Adverse events not covered elsewhere

For each selected category the reviewer had to describe the clinical context of the event and answer a series of more detailed questions about the circumstances surrounding the event. At the end of the questions for each category the reviewer was asked to indicate whether any system issues were of relevance and to describe these. Detailed descriptions of variables collected under each category are provided in Appendix 13.
3.12.5.8 Preventability assessment

A preventable adverse event was defined as “an event which results from an error in management and failure to follow accepted standards of practice”. (158) Accepted standard of practice was defined as “the current level of performance [in Ireland] that it is reasonable to expect from a practitioner who treats this type of problem”. (158) Preventability was judged by the physician reviewer using the same six-point scale as the Canadian Adverse Events Study. (16) To assist in this process the reviewer answered a structured series of questions designed to elicit any mitigating or aggravating factors:

- Is there a consensus regarding the diagnosis made in this case among Irish practitioners?
- Is there a consensus about the healthcare management in this case among Irish practitioners?
- How complex was this case?
- Was the management of the primary illness (not the adverse event) appropriate as compared to the Irish standard of practice?
- What was the degree of deviation of management of the primary illness (not the adverse event) from the Irish standard of practice?
- What was the patient’s level of co-morbidity?
- What was the degree of emergency in management of the primary illness (not the adverse event) prior to the occurrence of the adverse event?
- What potential benefit was associated with the management of the illness which led to the adverse event?
- What was the chance of benefit associated with the management of the illness which led to the adverse event?
- What was the risk of an adverse event related to the management?
- Is the injury/complication a recognised complication?
- What percentage of patients like this would be expected to have this complication?
The reviewer then rated on the below scale their confidence in the evidence for preventability and described the manner in which the adverse event was preventable (e.g. any strategies that could have prevented it):

1. Virtually no evidence of preventability
2. Slight to modest evidence for preventability
3. Preventability not quite likely; less than 50-50 but close call
4. Preventability more than likely; more than 50-50 but close call
5. Strong evidence for preventability
6. Virtually certain evidence for preventability

Adverse events judged as level four or greater out of six (i.e. at least: preventability more than likely; more than 50-50 but close call) were considered preventable. This was consistent with the Canadian Adverse Events Study.(16) The reviewer then assessed whether the adverse event was due to an act of omission or commission. Omission was defined as due to “inactions, i.e. failure to diagnose or treat”, and commission as due to “affirmative actions, i.e. incorrect treatment”.(158)

3.12.5.9 Outcome of the adverse event(s)

Once all the suspected injuries were reviewed the physician reviewer listed the overall outcomes for the patient. This involved selecting all the relevant outcome categories from a list of Major Clinical Categories (MCCs) based on the ICD-10 MCCs (Appendix 13).

3.12.5.10 Harm category

The physician reviewer indicated the maximum harm category for the patient using the same NCC MERP categorisation (E to I) that the nurse reviewers employed in stage-one. This was the most severe level of harm incurred by the patient as a result of healthcare management delivered either prior to, or during, the index hospitalisation. This concluded the stage-two review.
3.12.6 Reliability chart review
A warning box indicated that the chart was a reliability chart on submission of an original chart review. These charts were fully and independently reviewed by all nurse reviewers (stage-one review) and physician reviewers (stage-two review if the original chart had been triggered) working at the site. The review and data entry process were identical to the original review except the data was entered into the reliability databases. The appropriate database was selected by the reviewer on entering the study website.

3.13 Dataset and statistical analyses

3.13.1 Data cleaning and set up of datasets
The INAES web-based data collection populated five MySQL™ databases – one for original chart review data and four reliability databases. The datasets from these MySQL™ databases were exported into Excel spreadsheets and then imported into Stata® for data cleaning and analysis. Admission data from HIPE did not require data cleaning as it had undergone HIPE validation checks. Reviewer-entered fields that were missing were investigated by review of all the chart data entered for that admission and/or by reverting to the reviewer in question.

3.13.2 Adverse event determination
Injuries were categorised according to whether they resulted in disability and whether they were caused by healthcare management. Those that satisfied both conditions were determined to be adverse events. Adverse events were further examined according to the INAES location and timing criteria.

3.13.2.1 Disability
Disability was deemed to be present if the reviewer had indicated there was one or more of the following: disability on discharge, prolonged hospitalisation, death, subsequent hospitalisation. Injuries that did not involve
physical disability (e.g. the injury was of patient distress and/or prolonged hospitalisation alone) were not included in the main INAES analysis. This is because disability was defined as impairment of physical function.

3.13.2.2 **Causation**
Causation by healthcare management was deemed to be present if the reviewer had indicated that their level of confidence in causation by healthcare management was at least four on the six-point scale (management causation more likely (more than 50/50, but “close call”).

3.13.2.3 **Timing**
To be included as an adverse event in the INAES main analysis, the event had to have occurred either prior to the index admission and been detected within the index admission, or have occurred during the index admission and been detected either during this admission or after discharge.

3.13.2.4 **Location**
To be included as adverse event in the INAES main analysis, the event had to have occurred either in the index admission or in a related admission at the index hospital within 12 months prior to the index admission, i.e. in-hospital.

Note that as part of the comparison with international studies, adverse events with a lower level of healthcare management causation (≥2) or that occurred in out-of-hospital settings (e.g. primary care or a nursing home or another hospital outside of the hospital in which the index admission occurred) were included in the various adverse event eligibility scenarios.
3.13.3 Statistical analyses

All analyses were performed on Stata/IC® 13.1. Confidence intervals for binary variables were modelled using logistic regression; confidence intervals for incidence density were calculated using Poisson regression with robust variance estimation.

3.13.3.1 Weighted analyses

In order to maximise the number of adverse events reviewed the sample was stratified such that half of admissions had undergone a surgical procedure (without stratification this figure was approximately one quarter). The procedure codes for general anaesthetic, regional and neuroaxial blocks (ACHI 9251400-9251499, 9250800-9251299) were used as a proxy to indicate that surgery was likely to have been performed during the admission. Analyses were weighted for this sampling frame (i.e. the ratio of admissions with and without the anaesthetic procedure codes in each hospital’s eligible study population). For each hospital the total numbers of admissions with, and without, the procedure codes (“surgery” and “non-surgery”) were known as they were generated as part of the local HIPE random selection of admissions. These were used as the weights for each hospital. The Stata® command “svyproportion” produced the estimates of the weighted proportion of adverse events and weighted proportion of preventable adverse events.

3.13.3.2 Reliability analysis

Inter-rater reviewer reliability was analysed using the kappa statistic. For the nurse reviewer group, the outcome of interest was potential adverse event determination. The potential adverse event variable was automatically assigned as positive in the database when at least one of the 18 triggers was indicated as present by the nurse reviewer. For the physician reviewer group, the outcome of interest for inter-rater reliability was the presence of an adverse event. The variable indicating an adverse event was derived as positive in Stata® if all three of the following were present in the reviewed...
admission: (i) an injury; (ii) the injury resulted in disability, prolonged or subsequent hospitalisation, or death; and (iii) the healthcare management causation determination for the injury was at least four on the six-point scale.

3.13.3.3 Sensitivity of trigger screening for adverse events

Sensitivity is the “proportion of true positives that are correctly identified by the test”.(162) Two analyses were conducted of the stage-one trigger screening test. The first examined each trigger separately for its ability to identify adverse events. The second examined the whole stage-one trigger process and used review of trigger negative charts to establish the rate of false negatives.

Relative risks for each individual trigger (risk of an adverse event in the group with the trigger relative to the risk in those without the trigger) were generated using the Stata® “cs” command. Sensitivity and specificity values for the individual triggers and for the whole stage-one trigger screening process were calculated in Stata® using the “diagt” command.

3.13.3.4 Individual trigger sensitivity to detect adverse events

In this analysis, each of the stage-one triggers was the “test” under consideration. The physician reviewers’ determination of adverse event in triggered charts was considered to be the “gold standard” for the “disease” which the “test” is screening for.(30) Diagnostic test analysis was performed for each of the 18 triggers (e.g. trigger 1 present or not present, trigger 2 present or not present, etc.) individually.
3.13.3.5  Sensitivity of stage-one screening to detect adverse events

In this analysis, the entire stage-one determination of triggered, or not, by the nurse reviewers, was the “test” under consideration. Again the physician reviewers’ determination of adverse event was the “disease”.

I reviewed a sample of 196 trigger negative charts (mean of 24 per site) for adverse events. The proportion of adverse events found in the sample of trigger negative charts was used to estimate the number of false negative charts. This method was used in the Quality in Australian Health Care Study.(30)

3.13.4 Objective 1 What is the frequency and nature of adverse events for adult patients in major acute hospitals in Ireland?

This objective was achieved through analysis of the prevalence and incidence of adverse events in the INAES main dataset and examining the following factors: timing, disability and healthcare outcomes, length of stay, location and type of admission (elective or emergency).

3.13.4.1 Prevalence and incidence of adverse events

The prevalence of a disease is the number of cases in a defined population at a specified point of time, while its incidence is the number of new cases arising in a given period in a specified population.(148)

The INAES prevalence of adverse events in in-patient hospital admissions was calculated as the number of admissions associated with one, or more, adverse events divided by the number of admissions reviewed.(16) This was also referred to as the “risk” of an adverse event (i.e. risk of the admission being associated with an adverse event).
The INAES incidence density of adverse events was calculated as the number of adverse events occurring per 100 admissions. In this calculation events that occurred prior to the index admission were excluded to avoid double counting of events, i.e. only the occurrence of new events were included.

3.13.4.2 Length of stay
Length of stay for the index admission was calculated using the HIPE admission and discharge dates. The length of stay attributed to adverse events was calculated from the physician reviewer's estimate of the number of additional hospital days directly attributable to the adverse event under review.

3.13.5 Objective 2 How does the frequency and nature of adverse events for adult patients vary between the medical and surgical specialties in acute hospitals in Ireland?
This objective was achieved through analysis of the INAES main results according to medical and surgical specialty. Data on adverse event risk (prevalence) and type of event (clinical groupings as well as comparing events due to omissions and commissions) were examined.

The designation of medical or surgical was obtained from HIPE admission data using the HIPE specialty code assigned to the admission (i.e. the specialty assignment of the consultant associated with the principal diagnosis).(157) The surgical specialty group consisted of the following HIPE specialty codes: 600, 1400, 1700 – 1802, 2000, 2003, 2600, 2602, 2603, 2604, 7000, 7001, 7002, 7600, 7800, and 7802. The medical specialty group consisted of the following HIPE specialty codes: <500, 601 – 1302, 1503, 1600, 1900, 2300 – 2500, 2700, 2701, 5000, 7500, and 8003. Specialty codes for emergency department, palliative care, obstetrics and intensive care were not included in the medical or surgical specialty categorisations.
The data was also examined by the stratification groups of “surgery” and “non-surgery”. These were derived from the presence of procedure codes indicating that a surgical procedure was likely to have been performed during the admission (see section above on weighting).

3.13.6 Objective 3 What risk factors are associated with adverse events in major acute hospitals in Ireland?
This objective was achieved through analysis of the association of adverse event risk with age, sex and type of admission. Age was modelled as mean age and divided into ten year increments. Type of admission was grouped using data from HIPE obtained at the time of random selection of the INAES population: elective (HIPE admission types 1 and 2(157)) or emergency (all other HIPE admission types).

3.13.7 Objective 4 What proportion of adverse events identified by retrospective case note review is also identified by incident reporting?
Each hospital site was asked to provide the number and type of clinical adverse events they reported to the national incident reporting system, STARSweb (held by the CIS of the Irish State Claims Agency), in 2009. To calculate the adverse event incidences for each site the denominators from the local HIPE random selection search for admissions were used – total patients, total in-patients, total adult in-patients (aged at least 18 years and over). These were present on the screen shots taken of each stage of the HIPE search. This data was aggregated to give incidences for the hospitals as a group.

National reporting of clinical adverse events (STARSweb) data for 2009 was requested from the State Claims Agency.
3.13.8 Objective 5 What is the rate of preventable adverse events in Ireland?
An adverse event was considered “preventable” if it had a score of four or more on the six-point scale (i.e. a judgement of at least “preventability more than likely; more than 50-50 but close call”).(16) The proportion of INAES adverse events that were preventable was estimated, along with the distribution of preventability categories as determined by the physician reviewers. This data was analysed by hospital type. To establish the rate of preventable in-hospital adverse events, preventability was also estimated for events occurring in the index admission only.

3.13.9 Objective 6 What is the cost of adverse events to the Irish healthcare system?
National data for the cost analysis was provided by the Healthcare Pricing Office. This office was created in January 2014 from the National Case mix Programme and the Health Research and Information Division at the Economic and Social Research Institute.(163) The average bed-day cost of an in-patient hospital bed in Ireland in 2009 was €909.(153) According to the Healthcare Pricing Office this figure represents a fully absorbed cost: including treatment and care costs as well as “hotel” costs, but excluding capital and depreciation. The total of €909 relates to in-patients only and excludes day case, out-patient and emergency department costs. It was derived using diagnosis-related groupings (DRGs); cases which are clinically similar and are expected to consume similar amounts of resources are grouped into DRGs. This grouping, although mainly diagnosis driven, is carried out by examination of the case in its entirety including all diagnoses, all procedures carried out and demographic and administrative information. It is at this DRG level that costs per case are derived. It is not a cost at the procedure, diagnosis, ward or hospital level.
The number of adult in-patient admissions in 2009 excluding those with obstetric and psychiatric principal diagnoses was 339,844. To obtain this figure the Hospital In-Patient Enquiry Scheme at the Healthcare Pricing Office performed the same HIPE search strategy (i.e. to extract adult in-patients excluding those with obstetric and psychiatric principal diagnoses) that was conducted in the INAES HIPE databases on the 30 acute public hospitals reporting to HIPE in 2009 (Appendix 10).

The national cost of adverse events in adult in-patients was estimated as the product of (a) the estimated number of adverse events - using the INAES rate (weighted incidence density) of adverse events applied to the number of adult in-patient admissions in 2009, excluding those with obstetric and psychiatric principal diagnoses (n=339,844); and (b) the average cost of an event - calculated as the INAES mean number of additional bed days attributed to adverse events multiplied by the average cost of an in-patient hospital bed in Ireland in 2009 (€909 per day).

3.13.10 Objective 7 How does the Irish rate of adverse events compare with other international chart review studies?

The INAES adverse event rates were re-calculated using the different adverse event eligibility criteria (timing and location) that had been employed in other national retrospective chart review studies (and were outlined in the systematic review chapter). These are presented as five scenarios below:

3.13.10.1 Scenario 1: Include out-of-hospital events

This scenario includes all events associated with the index admission. Adverse events which occurred outside of the index hospital (i.e. out-of-hospital events) were included (for example, events where the healthcare was provided in primary care, at home, in nursing homes or other hospitals). An incidence cannot be calculated because the events may be associated
with admissions prior to the index admission as well as subsequent admissions. Therefore double counting of the number of events can occur.

3.13.10.2 **Scenario 2: Include events with any indication of management causation (≥2)**

This scenario includes events with a lower threshold of healthcare management than included in INAES. (30) In this scenario the INAES criteria for healthcare management causation was adjusted to include events scoring at least two on the two (instead of ≥ 4) on the six-point healthcare management causation scale (i.e. events must be judged as having at least slight to modest evidence of management causation). This was analysed in two ways – firstly, for all events (including events occurring outside of the index hospital, i.e. out-of-hospital events) and secondly, excluding out-of-hospital events.

3.13.10.3 **Scenario 3: Exclude out-of-hospital events**

This scenario includes all events associated with the index admission that occurred at the index hospital (16). Events relating to care outside the index hospital were excluded. This is the INAES prevalence. An incidence cannot be calculated because the events may be associated with admissions prior to the index admission as well as subsequent admissions. Therefore double counting of the number of events can occur.

3.13.10.4 **Scenario 4: Exclude events detected post index admission**

This scenario includes events detected in the index admission only. (2, 27, 32) Thus, INAES adverse events which occurred in the index admission, but were detected after discharge, were excluded.
3.13.10.5 **Scenario 5: Exclude events occurring pre index admission**
This scenario includes events occurring in the index admission only. (25) This timing was used for the INAES incidence density. Events occurring prior to the index admission were excluded.

3.13.11 **STROBE quality assessment**
The quality of the reporting of the INAES method and results in this thesis was assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, a tool for analysing the quality observational studies. (133) The STROBE statement is referred to in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals by the International Committee of Medical Journal Editors. The statement employs a checklist of 22 items that relate to the title, abstract, introduction, methods, results, and discussion sections of articles. A score of 22 indicates the highest quality of reporting.
3.14 Conclusion

The Irish National Adverse Events Study (INAES) was a two-stage retrospective patient chart review study. It was based on the Canadian Adverse Events Study which employed a modified version of the Harvard Medical Practice Study. All acute hospitals in the Republic of Ireland were invited to participate. Eight hospitals were randomly selected from those that agreed to participate, stratified by size and region. Three hundred adult in-patient admissions for 2009 were randomly selected from each site’s Hospital In-Patient Enquiry discharge database, excluding transfers and admissions with a psychiatric or obstetric principal diagnosis. Experienced nurse and physician reviewers were given standardised training in the two-stage chart review methodology. The INAES Operations Manual and web based data collection tool were adapted from the Canadian Adverse Events Study. Stage-one of the patient chart review involved nurse reviewers examining the index admission, and a year before and after, for a list of “triggers” indicating that an adverse event may have occurred. Triggered charts were reviewed by physician reviewers in stage-two to determine if an adverse event had occurred. To be an adverse event, an injury must have resulted in disability at discharge, prolonged hospitalisation or death, and be caused by healthcare management. Structured questions and six-point scales were used to assist physicians in their judgements of causation and preventability. Events must have occurred either prior to the index admission (and were detected in the index admission) or during the index admission. National data for demographic comparison and cost calculation was provided by the Healthcare Pricing Office. The prevalence of an admission being associated with an adverse event was calculated as the proportion of admissions with at least one adverse event. The incidence density was the number of events per 100 hospital admissions. To enable comparison with other international studies, the INAES results were re-calculated according to alternative criteria for event timing and location used by international retrospective chart review studies.
4 CHAPTER 4: RESULTS

4.1 INAES review process

4.1.1 Hospitals

All thirty acute public hospitals in the Republic of Ireland in 2009 were invited to participate in the Irish National Adverse Events Study (INAES). Eighteen out of thirty invited hospitals agreed to participate. Twelve hospitals did not agree: six refused and the remainder did not respond within the allocated timeframe despite a number of contacts. Of the 18 hospitals agreeing to participate, eight were randomly selected for the study. Random selection was stratified such that one large hospital and one small hospital were selected for each of the four regions of the Irish health system (HSE regions).

4.1.2 Patient charts

The majority of the patient charts across hospitals were paper-based or scanned paper records. In some sites reports or correspondence were available electronically but these tended to be a duplicate of documents included in the paper chart.

4.1.3 Study flow-chart of admissions

A total of 2,600 admissions were randomly selected from the hospitals’ HIPE discharge databases. Of the 2,600: 1,854 charts were screened for eligibility by the nurse reviewers and 1,609 (87%) were eligible for the study (Figure 4.1). The majority of ineligible admissions had been discharged with a hospital stay of under 24 hours (216/245=88%). A further 10% (25 out of 245) were ineligible because they were obstetric admissions which resulted in an uncomplicated birth. After excluding charts with inadequate documentation (26/1609=1.8%), 1,580 admissions underwent a full stage-one review, representing 188 - 201 admissions per hospital.
The physician reviewers excluded less than one percent (6/709=0.8%) of the 709 charts that progressed to stage-two review. Therefore 1,574 patient charts were fully reviewed in the Irish National Adverse Events Study.

Figure 4.1 Flow-chart of the INAES chart review process

*<24 hours: n=216; uncomplicated birth (n=25), transfer (n=2), not admitted (n=1), under 18 years old (n=1)
†<24 hours: n=1; uncomplicated birth (n=1), transfer (n=3), unable to locate (n=1)
4.1.4 INAES population

The 1,574 fully reviewed charts in INAES were comparable to national acute public hospital admissions in 2009 for age, sex, and length of stay (Table 4.1). Stratification ensured half of the INAES admissions had a procedure code indicating that it was likely surgery had been performed (the “surgery” group). Of the overall adult patient population admitted to acute public hospitals nationally, a higher proportion of national admissions were medical card holders (56% versus 51% in the INAES population); the significance of this is unclear but may be related to the greater proportion of surgical patients in INAES. The over representation of surgical patients in INAES is also likely to result in the presence of more elective patients (national data 20.4% versus 30.6% in INAES).

A lower proportion of the national admissions died during the admission (2.7% versus 4.8% of the INAES population). This is likely due to the INAES methodology excluding admissions with a hospital stay of less than 24 hours (unless death occurred within that time). It was only possible for this step to be performed by the nurse reviewers and not at the time of the HIPE search, so the exclusion is not represented in the national acute public hospital admissions. INAES therefore excluded a short-stay low-risk group while retaining all deaths; thus increasing the mortality rate. This exclusion step is also likely to be the reason for the INAES population having more elective admissions (exclusion of short-stay emergency admissions increases the proportion of elective admissions).
Table 4.1 Admission characteristics for national in-patients and INAES study population

*Adult in-patients excluding psychiatric and obstetric principal diagnoses (source: HIPE data from Healthcare Pricing Office, extracted using the INAES HIPE search strategy)
†INAES was stratified to select 50% “surgery” admissions

<table>
<thead>
<tr>
<th></th>
<th>National in-patients*</th>
<th>INAES population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of admissions</td>
<td>339,844</td>
<td>1,574</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>55.4</td>
<td>54.2</td>
</tr>
<tr>
<td>Female (%)</td>
<td>53.5</td>
<td>53.4</td>
</tr>
<tr>
<td>Medical card holder (%)</td>
<td>56.4</td>
<td>51.3</td>
</tr>
<tr>
<td>Elective (%)</td>
<td>20.4%</td>
<td>30.6%</td>
</tr>
<tr>
<td>“Surgery” (%)†</td>
<td>23.7</td>
<td>49.9</td>
</tr>
<tr>
<td>Died during admission (%)</td>
<td>2.7</td>
<td>4.8</td>
</tr>
<tr>
<td>Mean length of stay (days)</td>
<td>7.0</td>
<td>7.4</td>
</tr>
</tbody>
</table>

4.2 Stage-one review

Of charts reviewed, 45% were positive for one or more of the 18 triggers screened for by the research nurses in stage-one. The two triggers most frequently used were “unplanned readmission after discharge from index admission” and “unplanned admission before index admission”. The following triggers had the highest relative risks: “hospital acquired infection”, “unplanned return to the operating theatre”, and “unplanned removal/injury during surgery” with relative risks of 5.3, 4.8, and 4.7 respectively, and the greatest positive predictive values (Table 4.2). Fourteen of the triggers were separately associated with a statistically significant increased risk of an adverse event. The relative risks for three triggers – “cardiac or respiratory arrest”, “unplanned transfer to another acute care hospital” and “documentation and correspondence indicating litigation” – did not reach statistical significance. The trigger of “injury related to abortion or labour and delivery” was not deemed to be present in any chart.
Table 4.2 List of triggers ordered by frequency, percentage of charts positive for each trigger, relative risks (RR) with 95% confidence intervals (CI), and diagnostic test criteria

<table>
<thead>
<tr>
<th>Trigger number</th>
<th>Trigger description (ordered by frequency of triggering in INAES stage-one review)</th>
<th>% with trigger</th>
<th>RR (95% CI)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Unplanned readmission after discharge from index admission</td>
<td>18.5%</td>
<td>3.2 (2.5-4.0)</td>
<td>41.7%</td>
<td>85.1%</td>
<td>30.2%</td>
<td>90.4%</td>
</tr>
<tr>
<td>1</td>
<td>Unplanned admission before index admission</td>
<td>17.1%</td>
<td>2.5 (1.9-3.2)</td>
<td>33.6%</td>
<td>85.5%</td>
<td>26.4%</td>
<td>89.3%</td>
</tr>
<tr>
<td>18</td>
<td>Any other undesirable outcome not covered above</td>
<td>9.3%</td>
<td>2.7 (2.1-3.6)</td>
<td>21.8%</td>
<td>92.7%</td>
<td>31.5%</td>
<td>88.4%</td>
</tr>
<tr>
<td>9</td>
<td>Other patient complication (e.g. acute myocardial infarction, stroke, pulmonary embolism, any unexpected complication that is not a natural progression of disease or an expected outcome of treatment)</td>
<td>6.9%</td>
<td>3.7 (2.8-4.8)</td>
<td>21.3%</td>
<td>95.4%</td>
<td>41.7%</td>
<td>88.7%</td>
</tr>
<tr>
<td>15</td>
<td>Hospital-acquired infection or sepsis</td>
<td>6.5%</td>
<td>5.3 (4.3-6.7)</td>
<td>27.0%</td>
<td>96.7%</td>
<td>55.9%</td>
<td>89.5%</td>
</tr>
<tr>
<td>3</td>
<td>Hospital-incurred patient injury</td>
<td>5.5%</td>
<td>3.4 (2.6-4.6)</td>
<td>16.6%</td>
<td>96.3%</td>
<td>40.7%</td>
<td>88.2%</td>
</tr>
<tr>
<td>4</td>
<td>Adverse drug reaction</td>
<td>5.1%</td>
<td>2.7 (2.0-3.8)</td>
<td>12.8%</td>
<td>96.1%</td>
<td>33.8%</td>
<td>87.7%</td>
</tr>
<tr>
<td>16</td>
<td>Dissatisfaction with care documented in the medical record</td>
<td>2.5%</td>
<td>2.2 (1.3-3.6)</td>
<td>5.2%</td>
<td>97.9%</td>
<td>28.2%</td>
<td>87.0%</td>
</tr>
<tr>
<td>11</td>
<td>Unexpected death</td>
<td>1.3%</td>
<td>4.3 (2.8-6.5)</td>
<td>5.2%</td>
<td>99.3%</td>
<td>55.0%</td>
<td>87.1%</td>
</tr>
<tr>
<td>Trigger number</td>
<td>Trigger description (ordered by frequency of triggering in INAES stage-one review)</td>
<td>% with trigger</td>
<td>RR (95% CI)</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Positive Predictive Value</td>
<td>Negative Predictive Value</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------</td>
<td>-------------------</td>
<td>-------------</td>
<td>-------------</td>
<td>--------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>5</td>
<td>Unplanned transfer from general care to intensive care</td>
<td>1.2%</td>
<td>4.5 (3.0-6.7)</td>
<td>5.2%</td>
<td>99.4%</td>
<td>57.9%</td>
<td>87.1%</td>
</tr>
<tr>
<td>7</td>
<td>Unplanned return to the operating theatre</td>
<td>1.1%</td>
<td>4.8 (3.2-7.0)</td>
<td>5.2%</td>
<td>99.5%</td>
<td>61.1%</td>
<td>87.1%</td>
</tr>
<tr>
<td>12</td>
<td>Inappropriate discharge to home</td>
<td>&lt;1%</td>
<td>4.1 (2.5-6.9)</td>
<td>3.3%</td>
<td>99.6%</td>
<td>53.8%</td>
<td>86.9%</td>
</tr>
<tr>
<td>8</td>
<td>Unplanned removal, injury or repair of organ during surgery</td>
<td>&lt;1%</td>
<td>4.7 (3.0-7.4)</td>
<td>3.8%</td>
<td>99.6%</td>
<td>61.5%</td>
<td>87.0%</td>
</tr>
<tr>
<td>10</td>
<td>Development of neurological deficit not present on admission</td>
<td>&lt;1%</td>
<td>4.5 (2.7-7.3)</td>
<td>3.3%</td>
<td>99.6%</td>
<td>58.3%</td>
<td>86.9%</td>
</tr>
<tr>
<td>13</td>
<td>Cardiac or respiratory arrest</td>
<td>&lt;1%</td>
<td>2.1 (0.7-6.9)</td>
<td>0.9%</td>
<td>99.6%</td>
<td>28.6%</td>
<td>86.7%</td>
</tr>
<tr>
<td>6</td>
<td>Unplanned transfer to another acute care hospital</td>
<td>&lt;1%</td>
<td>0</td>
<td>&lt;1%</td>
<td>99.9%</td>
<td>&lt;1%</td>
<td>86.6%</td>
</tr>
<tr>
<td>17</td>
<td>Documentation or correspondence indicating litigation</td>
<td>&lt;1%</td>
<td>0</td>
<td>&lt;1%</td>
<td>99.9%</td>
<td>&lt;1%</td>
<td>86.6%</td>
</tr>
<tr>
<td>14</td>
<td>Injury related to abortion or labour and delivery</td>
<td>Not triggered</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
4.2.1.1 Individual trigger sensitivity to detect adverse events

The triggers with the highest sensitivities for detecting an adverse event were unplanned readmission after discharge (sensitivity 41.7%) and unplanned admission before the index admission (sensitivity 33.6%), but these had the lowest specificities of 85.1% and 85.5% (Table 4.2).

4.2.1.2 Sensitivity of stage-one screening

A review of trigger negative charts found adverse events in two out of 196 charts. This gave a 1.0% (95% confidence interval (CI) 0.1% - 3.7%) prevalence of missed charts. Thus, out of a total of 871 trigger negative charts, approximately nine admissions with adverse events could be false negatives (2/196 x 871 = 8.9). The relationship between the trigger screening (test) and physician review for adverse events (gold standard) is depicted in the two by two table below (Table 4.3).

<table>
<thead>
<tr>
<th>Trigger screening by research nurses (test)</th>
<th>Adverse event present</th>
<th>Adverse event not present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger positive (n=703)</td>
<td>211</td>
<td>492</td>
</tr>
<tr>
<td>Trigger negative (n=871)</td>
<td>9</td>
<td>862</td>
</tr>
</tbody>
</table>

The sensitivity and specificity of the trigger screening were calculated as 95.9% (95% CI 92.4% - 98.1%) and 64% (95% CI 61.0% - 66.2%). The positive predictive value of the trigger screening was 30.0% (95% CI 26.6% - 36.6%) and negative predictive value 99.0% (95% CI 98.0% - 99.5%).
4.3 Stage-two review

Six of the 709 patient charts that were triggered and progressed to physician review were subsequently excluded by the physician reviewers. The reasons for these exclusions were - three contained inadequate/missing documentation due to the index admission involving a transfer between hospitals, one was discharged with a hospital stay less than 24 hours, one admission was for an uncomplicated birth, and in one case the physician was unable to locate the patient chart. The physician reviewers therefore fully reviewed 703 patient charts.

4.3.1 Injuries

4.3.1.1 Disability

Out of the 703 patient charts, the physician reviewers identified 526 injuries in 374 admissions (more than one injury could be identified per admission). Fifteen of these injuries were excluded because they did not involve a physical disability (psychological distress or prolonged hospitalisation without physical injury were not included as adverse events because disability was restricted to impairment of physical function). This left 511 injuries in 363 admissions. Nearly two-thirds of these injuries (334/511=63%) satisfied the disability criterion for an adverse event (i.e. disability at discharge, prolonged or subsequent hospitalisation, or death).

4.3.1.2 Causation

The majority of the injuries identified (430/511=84%) were judged to be caused by healthcare management (at least four on the six point scale, i.e. management causation more likely (more than 50/50, but “close call”, or above). If the lower threshold was used for management causation (two on the six point scale, i.e. at least slight to modest evidence of management causation) then almost all the injuries were judged to have been caused by healthcare management (504/511=99%).
4.3.2 Adverse events

4.3.2.1 Timing of the AE
Of the 511 injuries, 291 (57%) satisfied the INAES disability and causation criteria and were therefore termed adverse events. These 291 adverse events occurred in 245 admissions. Two adverse events did not satisfy the timing criterion – one occurred and was detected prior to the index admission, and the other occurred and was detected after the index admission. Therefore 289 adverse events in 243 admissions remained.

Note if the lower threshold of ≥ 2 on the six-point causation scale had been used then 65% (331/511) of the injuries would have satisfied the disability and causation criteria. This group of injuries was included in one of the analyses for the international comparisons in Objective 7.

4.3.2.2 Location of the AE relative to the index hospital
The 289 adverse events which satisfied the disability, causation and timing definitions were examined for the location in which the adverse event occurred. Forty-two events occurred in locations outside of the index hospital, i.e. out-of-hospital events (with one additional event if the causation level was set to ≥2). These were not included in the main INAES analysis (but were included in the international comparisons under Objective 7). Thus the INAES main analysis included 247 adverse events in 211 admissions.
4.4 Objective 1 What is the frequency and nature of adverse events for adult patients in major acute hospitals in Ireland?

In stage-two, physician reviewers identified 247 adverse events in 211 admissions. This included 15% of admissions experiencing more than one adverse event.

4.4.1 Prevalence and incidence

The overall prevalence of an adverse event (i.e. the proportion of admissions associated with one or more adverse events) was 13.4% (95% CI 11.8% - 15.2%). After weighting for the sample frame of “surgery” to “non-surgery” patients the prevalence rate was 12.2% (95% CI 9.5% – 15.5%) (Table 4.4). The incidence density of adverse events was 11.9 events per 100 admissions (95% CI 10.2 - 13.7). The weighted incidence density was 10.3 events per 100 admissions (95% Poisson CI 7.5 – 13.1).

Table 4.4 INAES prevalence and incidence of adverse events

<table>
<thead>
<tr>
<th>Prevalence: risk of an admission being associated with an adverse event* (95% confidence interval)</th>
<th>Incidence density: number of adverse events per 100 admissions** (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude rate</td>
<td>211 admissions /1574 admissions = 13.4% (11.8% - 15.2%)</td>
</tr>
<tr>
<td>Weighted rate†</td>
<td>12.2% (9.5% - 15.5%)</td>
</tr>
</tbody>
</table>

*Includes events occurring prior to the index admission (and detected in the index admission) which were related to previous admissions at that hospital, and events occurring within the index admission (detected either during or after the admission)

**Excludes events occurring prior to the index admission

†Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame
4.4.2 Adverse event timing

Most (72.4%) of the adverse events occurred during the index admission (Table 4.5). This includes 48.9% which occurred and were detected during the index admission and 23.5% which were detected subsequently. Just over a quarter of events (27.7%) occurred prior to the index admission and were detected during the index admission. Hence, included adverse events spanned three timeframes but all had an association with the index admission (Table 4.5).

Table 4.5 The distribution of adverse events by the timing of occurrence and detection, with examples

<table>
<thead>
<tr>
<th>Weighted distribution (95% CI) of all study adverse events*</th>
<th>Timing of adverse event occurrence (O) and detection (D)</th>
<th>Example adverse event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before index admission</td>
<td>Index admission</td>
</tr>
<tr>
<td>48.9% (40.7% - 57.0%)</td>
<td>O</td>
<td>D</td>
</tr>
<tr>
<td>27.7% (19.9% - 37.0%)</td>
<td>O</td>
<td>D</td>
</tr>
<tr>
<td>23.5% (18.1% - 29.9%)</td>
<td>O</td>
<td>D</td>
</tr>
</tbody>
</table>

*Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame.
4.4.3 Adverse event disability outcome

Two-thirds (68%) of adverse events resulted in no physical impairment or disability at discharge, or in minimal to moderate impairment with recovery within 6 months (Table 4.6). Nonetheless, 10% of the adverse events resulted in permanent disability (e.g. ongoing neuropathic pain in a patient's leg following femoral-popliteal bypass), and 6.7% of adverse events (occurring in 14 patients) were felt by physician reviewers to have contributed to the patient’s death (Table 4.6). There was no statistically significant difference in risk of death in admissions that had adverse events (6.8% (95% CI 3.0% - 10.5%)) compared with admissions without events (4.9% (95% CI 2.9% - 6.9%), p=0.331).

Table 4.6 Distribution of degree of physical impairment attributable to the adverse event on the day of discharge

*Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame

<table>
<thead>
<tr>
<th>Degree of physical impairment attributable to the adverse event on the day of discharge</th>
<th>Number (%) of INAES events</th>
<th>Weighted distribution (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>31 (12.6%)</td>
<td>13.2% (9.2% - 18.6%)</td>
</tr>
<tr>
<td>Minimal impairment, or recovery in 1 month, or both</td>
<td>80 (32.4%)</td>
<td>33.6% (26.2% - 41.9%)</td>
</tr>
<tr>
<td>Moderate impairment, recovery in 1-6 months</td>
<td>54 (21.9%)</td>
<td>20.8% (15.9% - 26.7%)</td>
</tr>
<tr>
<td>Moderate impairment, recovery in 6-12 months</td>
<td>14 (5.7%)</td>
<td>5.0% (2.6% - 9.1%)</td>
</tr>
<tr>
<td>Permanent impairment, degree of disability ≤ 50%</td>
<td>23 (9.3%)</td>
<td>8.8% (5.1% - 15.0%)</td>
</tr>
<tr>
<td>Permanent impairment, degree of disability &gt; 50%</td>
<td>3 (1.2%)</td>
<td>1.1% (0.3% - 4.4%)</td>
</tr>
<tr>
<td>Death</td>
<td>15 (6.1%)</td>
<td>6.7% (3.3% - 12.9%)</td>
</tr>
<tr>
<td>Unable to determine</td>
<td>27 (10.9%)</td>
<td>10.9% (6.2% - 18.5%)</td>
</tr>
</tbody>
</table>
4.4.4 Adverse event healthcare outcome

Physician reviewers were able to select more than one healthcare utilisation outcome for each adverse event and 297 outcomes were selected for the 247 events. The most frequent outcomes were subsequent hospitalisation (51.8% of the 247 events), prolongation of hospital stay (37.7%) and disability at the time of discharge (16.6%) (Table 4.7).

<table>
<thead>
<tr>
<th>Outcome of the adverse event†</th>
<th>Number (%) of INAES events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subsequent hospitalisation</td>
<td>128 (51.8%)</td>
</tr>
<tr>
<td>Prolonged stay</td>
<td>93 (37.7%)</td>
</tr>
<tr>
<td>Disability at the time of discharge</td>
<td>41 (16.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>15 (6.1%)</td>
</tr>
<tr>
<td>Out-patient visits</td>
<td>13 (5.3%)</td>
</tr>
<tr>
<td>Other intervention/treatment without the sequelae listed above</td>
<td>7 (2.8%)</td>
</tr>
</tbody>
</table>

†Physician reviewers were able to select more than one category for each adverse event
4.4.5 Adverse event effect on index admission length of stay

Patients who experienced adverse events had a median length of index admission of seven days (inter-quartile range (IQR) 3, 17 days) compared with four days (IQR 2, 8) without adverse events (p<0.001). The difference in length of stay between patients with and without adverse events was evident even in admissions of short duration (Figure 4.2).

Figure 4.2 Relationship between length of stay and presence of an adverse event
4.4.6 Adverse event location

Over 80% of the 243 adverse events where a location was specified occurred in the patient’s ward or the operating theatre (Table 4.8). One event had two documented locations – the patient’s ward and an unknown outside of hospital location as there was insufficient detail about prior prescription of antibiotic therapy.

Table 4.8 Location of adverse event occurrence

*Includes one event with locations of the patient’s ward and an unknown out of hospital location.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number* (%) of adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s ward</td>
<td>121 (50.0%)</td>
</tr>
<tr>
<td>Operating theatre</td>
<td>85 (35.0%)</td>
</tr>
<tr>
<td>Emergency department</td>
<td>6 (2.5%)</td>
</tr>
<tr>
<td>Out-patient’s department</td>
<td>5 (2.1%)</td>
</tr>
<tr>
<td>Procedure room</td>
<td>4 (1.6%)</td>
</tr>
<tr>
<td>Radiology</td>
<td>4 (1.6%)</td>
</tr>
<tr>
<td>Another hospital</td>
<td>4 (1.6%)</td>
</tr>
<tr>
<td>Coronary care/Intensive care unit</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Physician’s office</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Ambulatory care unit/day ward</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Home</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Dental surgery</td>
<td>1 (0.4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (1.2%)</td>
</tr>
<tr>
<td>Total*</td>
<td>244</td>
</tr>
</tbody>
</table>
4.4.7 Adverse event type

Adverse events resulting from errors of omission (the failure to carry out necessary diagnosis or treatment, for example, delayed diagnosis of cancer due to failure to act on pathology report) were as common as those resulting from errors of commission (for example, hepatic duct injury during laparoscopic cholecystectomy surgery). The weighted frequency of errors of omission was 49.8% (95% CI 35.8% - 63.7%), with the corresponding frequency for errors of commission being 50.2% (95% CI 36.3% - 64.2%). The frequency of the different clinical types of adverse events is provided under Objective 2 according to medical and surgical specialty.
4.5 Objective 2 How does the frequency and nature of adverse events for adult patients vary between the medical and surgical specialities in acute hospitals in Ireland?

4.5.1 Adverse event risk in medical and surgical groups
The risk of an adverse event was higher in admissions with anaesthetic procedure codes (general anaesthetic, regional or neuroaxial blocks, the “surgery” group) indicating a surgical procedure was likely to have occurred, than in admissions without these codes (“surgery” 17.9% (95% CI 13.5% - 22.3%) versus “non-surgery” 10.2% (95% CI 7.2% - 13.1%); p=0.011).

However, when the 1,499 admissions with medical or surgical consultant speciality codes (allocated according to the admission’s principal diagnosis) were compared, there was no difference in event frequency between the specialities. The medical specialties had a weighted prevalence for admissions associated with adverse events of 11.9% (95% CI 8.3% - 15.5%) and the surgical specialties had a weighted prevalence of 13.1% (95% CI 9.8% - 16.5%), p=0.597.
4.5.2 Distribution of adverse events types for medical and surgical groups

The type of adverse event (categories were attributed by physician reviewers and an event could be attributed to more than one category) varied by speciality (medical or surgical – determined by consultant speciality codes allocated to the admission’s principal diagnosis). Surgical specialities had a greater proportion of operation-related events (occurring during surgery or within 30 days post-operatively), whereas therapeutic events (inappropriate or delay in treatment, or failure to monitor) and medication-related events were the dominant categories for medical specialities (Table 4.9).

Table 4.9 Type of event attributed to adverse events occurring in surgical and medical specialties by physician reviewer

*Physicians could attribute adverse events to more than one category

<table>
<thead>
<tr>
<th>Type of event*</th>
<th>Percentage of total adverse events for each specialty group*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Surgical (n=231)</td>
</tr>
<tr>
<td>Operation-related</td>
<td>45.5%</td>
</tr>
<tr>
<td>Therapeutic adverse event</td>
<td>18.2%</td>
</tr>
<tr>
<td>Drug/fluid-related</td>
<td>7.8%</td>
</tr>
<tr>
<td>Diagnostic event (wrong or delayed)</td>
<td>9.5%</td>
</tr>
<tr>
<td>Other event, not covered elsewhere</td>
<td>3.9%</td>
</tr>
<tr>
<td>Non-surgical procedure-related</td>
<td>3.5%</td>
</tr>
<tr>
<td>Fracture-related</td>
<td>6.9%</td>
</tr>
<tr>
<td>Anaesthetic-related</td>
<td>3.5%</td>
</tr>
<tr>
<td>Pregnancy-related</td>
<td>1.3%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
</tr>
</tbody>
</table>
These differences between medical and surgical specialties were striking when displayed as a bar graph (Figure 4.3).

![Classification of adverse events for medical and surgical specialties](image)

Figure 4.3 Frequency of adverse event types for medical and surgical specialties
However, when operation-related events were removed, the distribution of remaining event types was similar in medical and surgical specialties (Figure 4.4).

![Classification of adverse events excluding operation-related events for medical and surgical specialties](image)

Figure 4.4 Frequency of adverse event types (excluding operation-related events) for medical and surgical specialties

### 4.5.3 Acts of omission and commission for medical and surgical groups

There was no statistically significant difference between the medical and surgical specialties (determined by consultant speciality codes allocated to the admission’s principal diagnosis) in the percentage of events that were the result of omissions (medical specialties: 51.7% (95% CI 30.5% - 73.0%) versus surgical specialties 46.3% (95% CI 33.1% - 59.4%); p=0.627). There was also no statistically significant difference in percentage of events that were omissions between the “surgery” and “non-surgery” stratification groups (p=0.375). Note all events were classified as either omissions or commissions; therefore there were no statistically significant differences between the specialties regarding errors of commission.
4.6 Objective 3 What risk factors are associated with adverse events in major acute hospitals in Ireland?

4.6.1 Age and adverse event risk
Thirty-five percent of the patient sample in INAES reviewed charts was aged 65 years or over. The mean age of patients was significantly higher among admissions with an adverse event than those without (61.8 years versus 55.4 years; p<0.001 (t-test)) and with each ten-year increment in age there was an 18% increase in risk of an adverse event (OR 1.18, 95% CI 1.09 – 1.27). This clear progression of risk with age is shown in Table 4.10.

Table 4.10 Prevalence of adverse events according to ten year age groups
*Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Prevalence of an adverse event (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>6.9% (4.6% - 9.2%)</td>
</tr>
<tr>
<td>30-39</td>
<td>8.0% (5.8% - 10.3%)</td>
</tr>
<tr>
<td>40-49</td>
<td>9.3% (7.0% - 11.6%)</td>
</tr>
<tr>
<td>50-59</td>
<td>10.8% (8.4% - 13.2%)</td>
</tr>
<tr>
<td>60-69</td>
<td>12.5% (9.7% - 15.1%)</td>
</tr>
<tr>
<td>70-79</td>
<td>14.3% (11.5% - 17.6%)</td>
</tr>
<tr>
<td>80-89</td>
<td>16.5% (12.3% - 20.6%)</td>
</tr>
</tbody>
</table>
The smoothed curve in Figure 4.5 demonstrates how the older age groups have a higher burden of adverse events.

![Graph of age and adverse event risk](image)

Figure 4.5 Graph of age and adverse event risk

### 4.6.2 Sex and adverse event risk
There was no difference in adverse event risk between women (weighted prevalence 11.8% (95% CI 9.3% - 14.3%) and men (weighted prevalence 12.6% (95% CI 8.5% - 16.8%) (p=0.683, logistic regression).

### 4.6.3 Admission type and adverse event risk
The weighted prevalence of an adverse event was 12.6% (95% CI 9.3% - 15.9%) in elective admissions and 12.1% (95% CI 8.9% - 15.3%) in emergency admissions. The difference was not statistically significant (p=0.835, logistic regression).
4.7 Objective 4 What proportion of adverse events identified by retrospective case note review is also identified by incident reporting?

4.7.1 INAES hospital sites incident reporting

Data on clinical incident reporting was collected from half of the hospital sites. The other half of sites did not respond to requests for this information. Collection of this information was hampered by the change in information technology system from STARSweb to the National Adverse Events Management System (NAEMS) meaning that data from previous years was no longer accessible in the local hospital reporting systems.

The STARSweb notification guidelines require all incidents to be reported: a patient safety incident being “an event or circumstance which could have resulted, or did result, in unnecessary harm to a patient”.(165) Of the four hospitals that contributed data, one was only able to provide the total number of clinical incidents and another provided this number plus a graphical illustration of the distribution of type of event. Two gave a breakdown by incident type in numbers.

The leading type of event for the three hospital sites that were able to provide a breakdown of event type was slips/trips/falls. Other prominent categories were infection control incidents, medication incidents, and treatment incidents; these were in the top five for each hospital. It is important to note that these clinical incident reports represent all clinical incidents reported in all patients and settings (in-patients, out-patients, staff and persons on the hospital grounds) of the relevant hospital and include near misses. Therefore this figure cannot be compared to the INAES adverse event rates.
The denominators used for the calculation of incidence were the numbers of patients, in-patients and adult in-patients (aged at least 18 years and over) for 2009 for each hospital that provided reporting data. This was generated by the local HIPE search at the time of admissions sampling. Aggregated incidences are presented to ensure the hospital sites remain anonymous.

The clinical incident reports for 2009 from four of the INAES hospital sites therefore represented 5% of all their admissions (day cases and in-patients), 10% of the in-patients (including paediatric) and 11% of the adult in-patients.

4.7.2 National incident reporting

In 2011 there were 85,918 adverse events reported from all publically funded hospital and community healthcare organisations to the National Incident Management System (formerly known as STARSweb).(58, 165) The most frequent categories reported were consistent with the local hospital reporting data, i.e. mainly slips/trips/falls, medication incidents and treatment incidents, but with the addition of violence/harassment/aggression/abuse as the second most common category. The only denominator provided for this data is 4.5 million patient contacts which cover all HSE community and secondary care organisations.

Therefore, adverse events were reported in 1.9% of patient contacts in 2011. Again, this figure includes near miss events and the events can be reported for all persons on hospital and community healthcare grounds, i.e. not only for adult in-patients.

Data from 2009 was not available from the State Claims Agency because in 2014 the new system called the National Incident Management System, NIMS, was introduced (renamed in 2015 to NAEMS: National Adverse Event Management System). NIMS has different categorisations of incidents compared to STARSweb and therefore the State Claims Agency is not publishing historic incident data (personal communication, 22/9/2015).
4.8 Objective 5 What is the rate of preventable adverse events in Ireland?

4.8.1 Overall preventability

An adverse event was considered “preventable” if it had a score of four or more on the six-point scale (i.e. a judgement of at least “preventability more than likely; more than 50-50 but close call”, Table 4.11). An example of a preventable event was failure to prescribe anti-coagulant medication in a patient with a diagnosis of atrial fibrillation who was readmitted with right leg arterial embolism; a non-preventable example was a pneumothorax following computerised tomography (CT) guided biopsy of a lung mass resulting in overnight admission. Of the 247 adverse events, 179 (72.5%) were judged to be preventable. When these results were adjusted for the sampling strategy, 72.7% (95% CI 58.8% - 83.3%) of events were deemed preventable. Half (54%) of INAES events were in the two categories where the reviewer believed the judgement of preventability was a “close call” (Table 4.11).

Table 4.11 Distribution of level of preventability of adverse events

*Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame

<table>
<thead>
<tr>
<th>Rate on a 6 point scale your confidence in the evidence for preventability [an adverse event was considered ‘preventable’ if it had a score of four or more]</th>
<th>Number (%) of events</th>
<th>Weighted distribution (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Virtually no evidence of preventability</td>
<td>21 (8.5%)</td>
<td>9.6% (5.0% - 17.6%)</td>
</tr>
<tr>
<td>2. Slight to modest evidence for preventability</td>
<td>9 (3.6%)</td>
<td>3.6% (1.4% - 8.7%)</td>
</tr>
<tr>
<td>3. Preventability not quite likely; less than 50-50 but close call</td>
<td>38 (15.4%)</td>
<td>14.1% (8.8% - 22.0%)</td>
</tr>
<tr>
<td>4. Preventability more than likely; more than 50-50 but close call</td>
<td>95 (38.5%)</td>
<td>39.7% (33.3% - 46.4%)</td>
</tr>
<tr>
<td>5. Strong evidence for preventability</td>
<td>64 (25.9%)</td>
<td>24.8% (17.4% - 34.0%)</td>
</tr>
<tr>
<td>6. Virtually certain evidence for preventability</td>
<td>20 (8.1%)</td>
<td>8.3% (4.2% - 15.5%)</td>
</tr>
</tbody>
</table>
4.8.2 Preventability by hospital type

There was no difference between large and small hospitals in the risk of an adverse event or in the proportion rated as preventable (Table 4.12). The weighted adverse event risk for all hospital types was approximately 12%. Small hospitals had fewer preventable events than large hospitals (weighted percentages 68.1% versus 80.1%); however this difference was not statistically significant (p=0.254).

Table 4.12 Adverse event frequency, by hospital type

*Point estimates and confidence intervals were weighted to account for the sampling frame

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hospital type</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small</td>
<td>Large</td>
<td>All</td>
</tr>
<tr>
<td>Number of admissions sampled</td>
<td>792</td>
<td>782</td>
<td>1574</td>
</tr>
<tr>
<td>Number of admissions associated with an adverse event</td>
<td>108</td>
<td>103</td>
<td>211</td>
</tr>
<tr>
<td>Weighted adverse event risk (prevalence) (95% CI)*</td>
<td>12.4% (7.7% - 17.1%)</td>
<td>12.1% (8.5% - 15.7%)</td>
<td>12.2% (9.5% - 15.5%)</td>
</tr>
<tr>
<td>Number of adverse events</td>
<td>123</td>
<td>124</td>
<td>247</td>
</tr>
<tr>
<td>Number of incident adverse events (i.e. excluding events occurring prior to the index admission)</td>
<td>89</td>
<td>98</td>
<td>187</td>
</tr>
<tr>
<td>Weighted incidence of adverse events per 100 admissions (95% CI)*</td>
<td>9.5 (7.0 – 11.9)</td>
<td>10.8 (6.0 – 15.6)</td>
<td>10.3 (7.5 – 13.1)</td>
</tr>
<tr>
<td>Weighted percentage of adverse events that were preventable (95% CI)*</td>
<td>80.1% (68.7% - 91.5%)</td>
<td>68.1% (52.4% - 83.9%)</td>
<td>72.7% (58.8% - 83.3%)</td>
</tr>
</tbody>
</table>
4.8.3 Preventable in-hospital events
The weighted proportion of in-hospital events (events occurring in the index admission) that were preventable was 74.6% (95% CI 60.2% - 85.1%) compared with 72.7% (95% CI 58.8% - 83.3%) for all INAES events (includes pre-hospital events).
4.9 Objective 6 What is the cost of adverse events to the Irish healthcare system?

4.9.1 Additional cost of an adverse event in an admission

Physician reviewers attributed a mean of 6.1 (95% CI 4.7 - 7.7) additional hospital days to adverse events occurring in the index admission. These additional days could have taken place in the index hospitalisation or in a subsequent admission. This represented an additional cost of approximately €5,550 for each adverse event associated admission (i.e. 6.1 additional hospital days per event multiplied by €909 cost per day of an in-patient hospital stay\((153) = €5544.90\).

4.9.2 National cost of adverse events to the healthcare system

When extrapolated nationally, the estimated annual cost of hospital-based adverse events to the Irish healthcare system is €194 million (i.e. 10.3 events per 100 admissions, multiplied by 339,844 national admissions\((164) multiplied by €5544.90 equals €194,093,303).\)

Using the 95% confidence intervals for the mean attributable number of days for adverse events as a sensitivity analysis, the additional cost of each adverse event associated admission would range from €4272.30 to €6999.30. At national level, this estimates the corresponding national extrapolated annual costs at between approximately €150 million and €245 million.
4.10 Objective 7 How does the Irish rate of adverse events compare with other international chart review studies?

The INAES main results found a prevalence of adverse events of 12.2% (9.5% - 15.5%). (16) This risk was recalculated using the different adverse event timing and location criteria from the adverse event studies identified in the systematic review (chapter 2). The INAES re-calculations are described below and presented in Table 4.13.

4.10.1.1 Scenario 1: Include out-of-hospital events

If events caused by healthcare management outside the index hospital setting were included (e.g. events occurring in general practice, nursing homes or other healthcare facilities), the weighted risk of an admission being associated with an adverse event rose to 14.6% (95% CI 11.6% - 18.3%) (Table 4.13). (32, 33)

4.10.1.2 Scenario 2: Include events with any indication of management causation (≥2)

Employing a lower threshold to determine the likelihood of causation by healthcare management (i.e. a score of at least two out of the six-point scale), increased the weighted risk: 14.5% (95% CI 11.3% – 18.4%). (23, 30)

If events occurring outside of the index hospital were also included the weighted risk increased to 17.0% (13.4% - 21.3%).

4.10.1.3 Scenario 3: Exclude out-of-hospital events

This scenario is the INAES prevalence of 12.2% (95% CI 9.5% - 15.5%). It includes all events occurring in the index hospital which are associated with the index admission whether they occurred prior to, or were detected after, the index admission. This is based on the Canadian Adverse Events Study. (16) Events occurring in other healthcare settings outside of the index hospital (i.e. out-of-hospital events) were excluded.
4.10.1.4  **Scenario 4: Exclude events detected post index admission**
Exclusion of events occurring in the index admission and discovered subsequently, reduced the weighted adverse event risk to 9.4% (95% CI 7.4% - 11.9%).(2, 27, 32)

4.10.1.5  **Scenario 5: Exclude events occurring pre index admission**
Similarly exclusion of events prior to the index admission, resulted in a weighted risk of 8.6% (95% CI 6.7% - 10.9%).(25)
Table 4.13 Weighted frequency of INAES adverse events with the application of international adverse event eligibility criteria

N/A = Not Applicable, i.e. unable to calculate an incidence as including events occurring in admissions prior to the index admission, as well as events detected in admissions after the index, will result in double counting; † Point estimates and confidence intervals (CIs) were weighted to account for the sampling frame

<table>
<thead>
<tr>
<th>Adverse event (AE) eligibility criteria (timing and location)</th>
<th>Number of admissions with AEs (number of events)</th>
<th>Crude risk prevalence (95% CI)</th>
<th>Weighted risk prevalence (95% CI)</th>
<th>Crude incidence density (95% CI)</th>
<th>Weighted incidence density (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scenario 1: All AEs</td>
<td>243 (289)</td>
<td>15.4% (13.7% - 17.3%)</td>
<td>14.6% (11.6% - 18.3%)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Scenario 2:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i) Include all events with any indication of management causation (≥2)</td>
<td>277 (331)</td>
<td>17.6% (13.4% - 21.3%)</td>
<td>17.0% (13.4% - 21.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii) As previous but exclude out-of-hospital events</td>
<td>245 (288)</td>
<td>15.6% (13.9% - 17.4%)</td>
<td>14.5% (11.3% - 18.4%)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Scenario 3: Exclude out-of-hospital events</td>
<td>211 (247)</td>
<td>13.4% (11.8% - 15.2%)</td>
<td>12.2% (9.5% - 15.5%)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Scenario 4: Exclude events detected post index</td>
<td>157 (183)</td>
<td>10.0% (8.6% - 11.6%)</td>
<td>9.4% (7.4% - 11.9%)</td>
<td>11.6 events per 100 admissions (10.0 – 13.4)</td>
<td>10.9 events per 100 admissions (8.2 – 13.7)</td>
</tr>
<tr>
<td>Scenario 5: Exclude events occurring pre index</td>
<td>156 (187)</td>
<td>9.9% (8.5% - 11.5%)</td>
<td>8.6% (6.7% - 10.9%)</td>
<td>11.9 events per 100 admissions (10.2 – 13.7)</td>
<td>10.3 events per 100 admissions (7.5 – 13.1)</td>
</tr>
</tbody>
</table>
The INAES prevalence and incidence results were then compared with the equivalent results from other international studies (excluding rates from prospective and cross-sectional studies). The weighted INAES adverse event rates and the range for the other international retrospective chart review studies are presented below (Table 4.14):

1. include all adverse events: INAES 14.6%, international range 7.6%(20) - 12.3%(33)

2. include events with a low threshold for causation: INAES 14.5% (or 17.0% if out-of-hospital events are included), international range 5.4%(27, 122) - 16.6%(30)

3. exclude events occurring outside of the index hospital: INAES 12.2%, international range 4%(126) - 8.6%(48)

4. exclude events discovered after the index admission: INAES 9.4%, international range 2.9%(27) - 10.6%(122)

5. exclude events occurring prior to the index admission: INAES 9.9%, international range 8.8%(166) - 11.1%(25)

4.11 STROBE quality assessment

A STROBE checklist was completed for this thesis (Appendix 14). All items were present giving the thesis a score of 22 out of 22.
Table 4.14 INAES and adverse event rates from other international retrospective chart review studies (adjusted rates in brackets)

NZ=New Zealand; ‡Egypt, Jordan, Kenya, Morocco, South Africa, Sudan, Tunisia, Yemen. †Three Dutch studies

<table>
<thead>
<tr>
<th>AE eligibility criteria</th>
<th>Ireland</th>
<th>USA (2)</th>
<th>Australia (30, 122, 166)</th>
<th>USA (27, 122)</th>
<th>England (28, 166)</th>
<th>NZ (32, 139, 166)</th>
<th>Canada (16)</th>
<th>Scotland (34)</th>
<th>Spain (14)</th>
<th>England (23)</th>
<th>Sweden (33)</th>
<th>Brazil (50)</th>
<th>Tunisia (44)</th>
<th>Africa‡ (29)</th>
<th>Italy (24)</th>
<th>PortugaI (25)</th>
<th>The Netherlands (126)†</th>
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<tr>
<td>1: All AEs</td>
<td>15.4% (14.6%)</td>
<td>11.3%</td>
<td>9.3%</td>
<td>12.3%</td>
<td>7.6%</td>
<td>10.5% (range 7.7-13.1%)</td>
<td>10%</td>
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<td>2: Include AEs ≥2 causation</td>
<td>15.6% (14.5%) [or all AEs 17.6% (17.0%)]</td>
<td>16.6%</td>
<td>5.4%</td>
<td>12.9% (13.1%)</td>
<td>10.9%</td>
<td>6.8% (7.5%)</td>
<td>8.4%</td>
<td>8.6%</td>
<td>4%, 6%, 5.7%</td>
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<tr>
<td>3: Exclude out-of-hospital AEs</td>
<td>13.4% (12.2%)</td>
<td>4.2%</td>
<td>6.8% (7.5%)</td>
<td>8.4%</td>
<td>8.6%</td>
<td>10.0%</td>
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<td>4: Exclude AEs post index</td>
<td>10.0% (9.4%)</td>
<td>3.7%</td>
<td>10.6%</td>
<td>2.9% (3.2%)</td>
<td>10.0%</td>
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<tr>
<td>5: Exclude AEs pre index</td>
<td>9.9% (8.6%)</td>
<td>10.8%</td>
<td>8.8%</td>
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<td>No AE criteria given</td>
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4.12 Conclusions

The Irish National Adverse Events Study reviewed 1,574 patient charts. The screening stage (stage-one) of the INAES methodology had a high sensitivity (for detecting charts containing adverse events) of 96%. The prevalence of adverse events in adult in-patients of Irish acute public hospitals was 12.2%. This represented an incidence density of 10.3 adverse events per 100 admissions. Over two-thirds of adverse events resulted in no or minor impairment, although 6.7% were associated with death. Hospital readmission and prolonged hospital stay were the most frequent healthcare outcomes of adverse events. Errors of omission were as common as errors of commission. Adverse event risk was highest in those who had procedure codes indicating surgery was likely to have been performed. However, when the data was analysed according to the specialty code of the principal diagnosis, there was no difference in risk between medical and surgical specialties. The distribution of type of event depended on whether surgery had been performed and, if so, then the major category was operation-related events; otherwise most events were therapeutic-related, medication-related or diagnostic events. Increasing age, but not sex or type of admission (elective or emergency), was associated with a greater risk of an adverse event. The INAES results were unable to be compared to hospital incident reporting because of the lack of information in the latter regarding the distribution of adverse events and near misses and the proportion of events reported in in-patients. A high proportion (72.7%) of adverse events was judged to be preventable. Each adverse event resulted in an additional 6.1 days and €5550 cost, which, when extrapolated nationally represented an expenditure of between 150 and 245 million euro. The INAES risk of an adverse event varied between 8.6% and 17.0% if different criteria (employed in other international patient chart review studies) were used to identify the adverse events.
5 CHAPTER 5: DISCUSSION

5.1 Summary of thesis findings

Patient safety came to prominence after the publication of the *To Err is Human* report in 1999. This led to a systems approach and promotion of a safety culture in healthcare. Large adverse event studies reviewing hospital patient charts have estimated that adverse events occur in between 3% and 17% of admissions, with one- to two-thirds of these being preventable. Most adverse events are mild, but approximately 14% cause permanent harm or contribute to death. Adverse events result in longer hospital stays and are a significant cost to the healthcare sector. Adverse events are captured through a variety of methods but only systematic collection in a population can be used for healthcare quality reporting of adverse event. This is not being achieved in the Republic of Ireland currently, and there is no national information on the incidence and prevalence of adverse events. The Harvard Medical Practice Study retrospective methodology of two-stage patient chart review was chosen for the Irish National Adverse Events Study due to its high sensitivity, use in other international studies and ability to assess preventability.

The systematic review of adverse event studies conducted as part of this thesis highlighted differences between international adverse event studies in many methodological aspects, including: study population, threshold criteria for causation and preventability, extent of documentation reviewed, number of reviewers per chart and the timing and location criteria for adverse event eligibility. All of these factors need to be taken into account when comparing the results from the Irish National Adverse Events Study with other adverse event studies. Apart from age and sex, very little data were extracted describing adverse event risk in terms of patient characteristics. Results focussed on hospital environment factors such as type of admission, location of adverse event, and responsible department. Sex was not associated with a difference in adverse event risk. Increasing age was associated with increased risk of an adverse event. It is likely that the presence of co-
morbidity also increased risk, but comparison was difficult as a standard method was not used to examine this.

The Irish National Adverse Events Study used a two-stage retrospective patient chart review design. It was based on the Canadian Adverse Events Study which employed a modified version of the Harvard Medical Practice Study. All acute hospitals in the Republic of Ireland were invited to participate. Eight hospitals were randomly selected from those that agreed to participate, stratified by size and region. Three hundred adult in-patient admissions for 2009 were randomly selected from each site’s Hospital In-Patient Enquiry discharge database, excluding transfers and admissions with a psychiatric or obstetric principal diagnosis. Experienced nurse and physician reviewers were given standardised training in the chart review methodology. Stage-one of the patient chart review involved nurse reviewers examining the index admission and a year before and after for a list of “triggers” indicating that an adverse event may have occurred. Triggered charts were reviewed by physician reviewers in stage-two to determine if an adverse event had occurred. To be an adverse event an injury must have resulted in disability at discharge, prolonged hospitalisation or death, and be caused by healthcare management. Structured questions and six-point scales were used to assist physicians in their judgements of causation and preventability. Events must have occurred either prior to the index admission (and were detected in the index admission) or during the index admission. National hospital discharge data for demographic comparison and cost calculation were provided by the Healthcare Pricing Office. The prevalence of an admission being associated with an adverse event was calculated as the proportion of admissions with at least one adverse event. The incidence density was the number of events per 100 hospital admissions. To enable comparison with other international studies, the INAES results were re-calculated according to alternative criteria for event timing and location used by similar retrospective chart review studies identified in the systematic review.
The Irish National Adverse Events Study reviewed 1,574 patient charts. The screening stage (stage-one) of the INAES methodology had a high sensitivity (for detecting charts containing adverse events) of 96%. The prevalence of adverse events in adult in-patients of Irish acute public hospitals was 12.2% with an incidence density of 10.3 adverse events per 100 admissions. Over two-thirds of adverse events resulted in no, or minor impairment, although 6.7% were associated with death. Hospital readmission and prolonged hospital stay were the most frequent healthcare outcomes of adverse events. Errors of omission were as common as errors of commission. Adverse event risk was highest in those who had procedure codes indicating surgery was likely to have been performed. However, when the data was analysed according to the specialty code associated with the principal diagnosis, there was no difference in risk between medical and surgical specialties. The distribution of type of event depended on whether surgery had been performed and, if so, then the major category was operation-related events; otherwise most events were therapeutic-related, medication-related or diagnostic events. Increasing age, but not sex or type of admission (elective/emergency), was associated with a greater risk of an adverse event. The INAES results were unable to be compared to hospital incident reporting because of lack of information in the latter regarding the distribution of adverse events and near misses and the number of events reported in in-patients. A high proportion (72.7%) of adverse events was judged to be preventable. On average, each adverse event resulted in an additional 6.1 days in hospital and an additional cost of €5,550 which, when extrapolated nationally, represented an expenditure of between €150 million and €245 million. The INAES risk of an adverse event varied between 8.6% and 17.0% if different criteria (employed in other international patient chart review studies) were used to identify the adverse events.
5.2 The frequency and nature of adverse events for adult patients in major acute hospitals in Ireland

The INAES prevalence and incidence results provide for the first time information to the Irish healthcare system on the burden of adverse events in Irish hospitals. The INAES estimated an adverse event prevalence rate of 12.2% in hospital in-patient admissions and an incidence of 10.3 events per 100 admissions. At a national level this extrapolated to approximately 41,500 out of 340,000 adult admissions (excluding obstetric and psychiatric) to Irish acute public hospitals in 2009.

The 12.2% prevalence rate (risk of an admission being associated with an adverse event) provides an estimate of the admission-related adverse event burden in hospitals. It includes adverse events occurring prior to the admission as well as those detected in subsequent admissions. Only one adverse event is counted per admission but each adverse event can be associated with more than one admission over time. The prevalence rate thus describes the relationship between the risk of adverse events and hospital admissions in general, but does not provide information on the number of events. If events in primary care and community healthcare settings were included, the risk would increase to 14.6% and represent the additional burden to hospitals of adverse events in the Irish healthcare system.

The adverse event incidence density of 10.3 events per 100 admissions provides an indication of the event-related adverse event burden occurring in hospitals. It counts all adverse events that occur during admissions. The incidence represents the de novo occurrence of adverse events for hospitals. These are the events that hospitals are directly responsible for. Policy makers focussing on reducing the incidence of adverse events in hospital services should target this as the baseline rate of adverse events occurring within admissions.
The leading categories of events by frequency in INAES were similar to other studies internationally: operation-related, therapeutic, medication-related and diagnostic.(16, 27, 32) Most adverse events did not cause permanent disability or harm; however even mild events caused significant and costly additional bed days. In INAES, 6.7% of adverse events were judged to have potentially contributed to death; in other studies this ranged from approximately 4%(14, 30) up to 30%(16, 29). The overall rate of admissions associated with death in INAES was 0.9% (=14/1574, weighted 0.8% 95% CI 0.4% - 1.7%), which is in line with similar findings in international research (Canada 1.6%,(16) the Harvard Medical Practice Study 0.5%,(2) and Australia 0.8%(30)). However, no additional information was collected about expected life expectancy without the adverse event. Eighty-five percent of adverse events in INAES occurred in the patient’s ward or operating theatre, consistent with other adverse event studies.(30)

5.3 Variation in the frequency and nature of adverse events for adult patients in medical and surgical specialities in acute hospitals in Ireland

Patients undergoing surgery had a higher risk of adverse events than those who did not have surgery during the admission. This is consistent with other studies and is not surprising given the complexity and number of decision makers and technology involved in a surgical procedure.(35) However despite this (and in contrast to other research), INAES found that patients cared for under a surgical consultant (i.e. their principal diagnosis had a surgical specialty code) had a similar risk of adverse events in their admission compared to those under a medical consultant. This is probably due to admission procedures in Irish hospitals: approximately a quarter of admissions with a HIPE surgical speciality code did not appear to have had surgery (as judged by the absence of a procedure code for an anaesthetic likely to be associated with surgery); whereas, approximately 5% of admissions with a medical speciality code had procedure codes indicating that the patient underwent surgery during the admission. This would be
different to other healthcare systems, for example Canada, where only patients undergoing surgery are admitted under a surgical consultant. The distribution of type of event was similar between medical and surgical specialties if operation-related events were removed. Information bias should be considered when interpreting these results. Surgery is accompanied by a high degree of documentation – operation notes, intra and post-operative measurements, fluid balance and pain management. Therefore it is possible that the retrospective chart review methodology is better at identifying operation-related events than other types.

5.4 Risk factors associated with adverse events in major acute hospitals in Ireland

The INAES showed that older patients were more at risk of adverse events. This is consistent with other studies internationally as shown in the systematic review performed in chapter 2. However the reasons for this increase in risk are likely to be multi-factorial. For example, increased risk of adverse events may be a result of the increased vulnerability of patients due to the presence of more co-morbidities (more complicated disease) and/or longer hospital stays and/or multiple treatments.\(^\text{(11)}\) Thus, older patients are likely to have a greater exposure to risk.\(^\text{(13)}\) Analysis of the Utah/Colorado study found that the elderly had a higher rate of preventable adverse events but age was not an independent predictor after adjusting for co-morbidity and case mix.\(^\text{(26)}\) No difference in risk was found for gender in INAES and this is consistent with other studies internationally, as demonstrated in the systematic review.

The INAES did not find a difference in adverse event rates with hospital size, unlike the Canadian study.\(^\text{(16)}\) However, hospital categorisation necessarily relates to local demographic, geographic and health service factors and was different between the studies.\(^\text{(16)}\). In both studies, the method of hospital categorisation used a combination of actual numbers (beds or case mix
units) plus factors indicating a higher referral centre (university hospital, National Cancer Centre). In addition, there is no internationally recognised method of categorisation of hospitals that is able to fully account for differences in acuity, transfer of patients, complexity of care (number of healthcare providers involved), quality of documentation and general quality of care. (16)

5.5 The proportion of adverse events identified by retrospective case note review also identified by incident reporting

The Irish national public healthcare reporting system has a very low rate of adverse event reporting. In 2011, adverse events were reported by hospital and community healthcare organisations in 1.9% of patient contacts using the National Incident Management System (NIMS, formerly known as STARSweb). (58, 165) Limited analysis of this data was able to be performed because the State Claims Agency only releases aggregated event totals without detail on the setting (hospital versus community) or severity of event (adverse events compared with near misses). In addition, national reporting data from 2009 was not available, because in 2014, a new information technology system (NIMS) was introduced with different categorisations of incidents compared to STARSweb. The State Claims Agency has therefore decided not to publish historic incident data. Thus, the current system of national reporting does not allow for calculation of in-patient adverse event rates or tracking of rates over time.

Four of the INAES hospitals provided the research team with their adverse event reporting data for the year 2009. Two of the four were only able to state the total number of events they reported to the CIS and two were able to additionally provide the type of event. No figures were available regarding adverse event setting and location (in-patients, day cases, out-patients, emergency department, or hospital grounds) or severity (near misses or adverse events). The aggregated rate of reporting of 5% of all admissions
therefore provides very little information on which to determine patient safety policy or interventions. It is also not possible to compare this data to the INAES adverse event rates because of uncertainties in both the numerator and the denominator in the data reported to the CIS.

Thus, at a minimum there is under-reporting of adverse events in the Irish healthcare system and also a significant knowledge gap in the detail available about what is being reported. This under-reporting is consistent with other research which has found that incident reporting captures 3 - 10% of events compared to retrospective chart review.(34, 108) Reasons for this include lack of awareness or belief in the value of reporting, fear of litigation, and lack of a supportive culture encouraging reporting.(60, 78) Irish research has also shown that most reports are from nurses.(60) Reporting to the CIS National Adverse Events Management System is not anonymous and this may affect reporting patterns. In order to encourage a reporting culture with involvement of all healthcare professionals there will need to be significant improvement in the patient safety culture in Irish healthcare, as well as in other health systems, with a move to a no-blame culture in contrast to what currently exists in healthcare. This should include feedback to adverse event reporters, all healthcare workers and managers about adverse event rates overall, with greater depth of information provided so that interventions and policies can be developed to enhance patient safety.

5.6 The rate of preventable adverse events in Ireland
Over 70% of INAES adverse events were considered preventable. This appears high compared with a previous systematic review aggregate estimate of 43.5%.(35) in international studies. However, the range of events falling within the definition of preventability is likely to increase over time with advances in surgical techniques, therapeutics and quality initiatives, and more recent studies have reported similarly increased rates of events deemed “preventable”.(11, 29, 33, 167) Indeed, one recent adverse events study attributed their high preventability rate of 70% partly to the physician
reviewers being able to compare findings with each other, enabling more complete retrieval of information and aiding interpretation. (33) Physician reviewers in the INAES were also encouraged to discuss cases together.

Preventability was assessed by the physician reviewers based on standards at the time of the admission and rated using a six-point scale. Preventability was dichotomised for purposes of analysis, the 72.7% figure for INAES reflecting this dichotomised preventability rating. However, over half of the events in the INAES were rated in the middle “close call” 50:50 zones. This is indicative of the difficulty for reviewers in preventability assessment. In many cases standards of practice may not be well defined, so that preventability is easier to define for events with guidelines or standards, but difficult to judge for those without.

Over 70% of both in-hospital and all INAES adverse events were judged to be preventable. Preventable in-hospital events are de novo events occurring in hospitals that are avoidable and therefore should be targeted by hospitals for monitoring and intervention. (139) These events also provide a measure of quality of care that is not affected by level of service provision (e.g. factors influencing access to services) as the patients have all been admitted to hospital. (140)

5.7 The economic cost of adverse events to the Irish healthcare system
The cost of adverse events is significant not only in terms of adverse outcomes for patients but also the trauma and consequences of the event for all involved – patients, families and staff. (66) Financially, an annual cost of €200 million represents approximately 4% of the Irish healthcare acute services 2009 budget of €5,288,000. (168)
The INAES calculation of cost for Ireland is similar to other research. The report *To Err is Human* used data from the original Harvard Medical Practice Study to estimate that adverse events accounted for 4% - 6% of national expenditure on health.(1) In the Netherlands 1% of healthcare spending is thought to be on preventable adverse events.(31) In monetary terms estimated costs of adverse events have included NZ$1.6 billion in New Zealand in 1998, £1billion pounds for preventable events in England and Wales in 2001 and $4.7 billion in Australia in 1995.(28, 30, 75) The Netherlands calculated that in 2004 adverse events cost €355 million and preventable adverse events €161 million in direct medical costs.(73) The Dutch and New Zealand cost analyses of their chart review studies included excess length of stay (bed days attributable to the adverse event) and additional procedures (for each adverse event physician reviewers documented whether additional treatments or interventions were necessary) in their calculation of costs.(73, 75)

The INAES cost figures are almost certainly an underestimate as it does not take into account costs such as escalation of care (transfer to a higher dependency unit, further operations, or other treatment resulting from an adverse event), additional out-patient visits, societal costs (absence from work, premature death or disability) and litigation. Also the average cost of a bed day after an adverse event is likely to be more expensive due to interventions and/or transfer to higher dependency being required in some cases.(41, 73) Furthermore, day cases, emergency department assessments, paediatric, and the majority of obstetric and psychiatric admissions were not included in INAES, and so a total cost of adverse events for all hospital patients in the Republic of Ireland cannot be not provided.
Cost in INAES was only calculated by the mean additional length of stay attributed to the adverse events. The Utah and Colorado study estimated healthcare costs to contribute approximately half (52.6%) of the total costs of adverse events, with the remainder due to time off work, lost household productivity, and cost of disability. Of the healthcare costs in-patient days represented only 43% (57% was attributed to out-patient care; in particular, nursing home care). Therefore the cost to Ireland of adverse events (€194million) may be more than double what was calculated with the INAES data. For example, if in-patient costs contributed 43% of adverse event-related healthcare costs, one could estimate that Ireland’s total healthcare costs would be €451million (= €194/0.43). This represents 9% of the total healthcare expenditure of €5,288,000 in 2009. If non-healthcare costs were then included the total cost of adverse events would rise to €857million per annum (= €451/0.527).

5.8 The rate of adverse events in Irish hospitals compared with other international chart review studies

The INAES adverse event prevalence of 12.2% and incidence of 10.3 events per 100 admissions fall within the range of other international studies (2.9%(27) - 16.6%(30)) and are most similar to those of the United Kingdom and New Zealand. However, the systematic review in chapter 2 highlighted that many of the international adverse event studies used different eligibility criteria for adverse event location (out-of-hospital and in-hospital events) and timing (occurring prior to the index admission or detected after the index admission). When the INAES data were examined for the effect of applying these various criteria, the INAES adverse event rate varied from 8.6% to 17.0%, i.e. ranging from a 20% decrease to a 40% increase in risk. This variation in criteria within the Harvard Medical Practice Study methodology makes it difficult to assess whether there were intrinsic differences in adverse event occurrence between healthcare systems. However, the
INAES re-calculations have made it possible to compare adverse event frequencies between countries which have employed different criteria. The international rates ranged from under 3% (74) where only events detected during the index admission were included to approximately 17% (30) with inclusion of all events (out-of-hospital and in-hospital) and use of a lower threshold to determine causation by healthcare management.

These discrepancies in adverse event criteria highlight the challenges inherent in the systematic measurement of adverse events, even if a similar methodology (the Harvard Medical Practice Study) is employed. Part of the issue also appears to be lack of clarity about whether the study rate being presented is an incidence or prevalence rate. For example, the original Harvard Medical Practice Study incidence rate includes only those events discovered during the index admission whereas the Canadian Study’s incidence rate includes events discovered in the index admission as well as in subsequent admissions and as such, is a better measure of prevalence because all events associated with admissions are included. (2, 132) The Australian study proposed correcting the adverse event rate for events that were related to several admissions. They assumed the ratio of adverse events per admission is 80% of the proportion of admissions with adverse events. (30) This would adjust the INAES risk from 12.2% to 9.8%, which is similar to the 9.9% incidence calculated using the INAES incident events only (i.e. events occurring in the index admission, no pre-hospital events).

Less easily quantified are other differences between studies which mean that comparisons between studies using the Harvard Medical Practice Study methodology should be made with caution. Importantly, quite different populations were studied in the various national adverse event studies. The earlier systematic review showed that the hospital population studied varied in terms of whether or not they included paediatric, short stay, psychiatric and/or obstetric patients. These differences alone will result in age and other demographic variability between populations studied. The Swedish study had
a higher proportion of elderly (48% were aged 65 years or over) than other studies - Australia (28%), New Zealand (30%), New York (17%), and the Danish study (32%). (2, 32, 33, 49) In INAES this proportion was 35%. Comparisons are also difficult in the same setting over time, as even if the same hospital is studied there may be changes in patient profile and hospital practices over time. For example, the Netherlands researchers demonstrated a statistically significant increase in age and length of stay between their 2004 and 2008 studies. (126)

There are other methodological differences between the various international studies. The systematic review showed that studies used slightly different trigger lists and had different rates of triggered charts (ranging from 8% (24) to 62%; (18, 22) compared to 45% in INAES). Thus the proportion of charts that were assessed by a physician varied significantly and this may affect the resultant adverse event rate. For example, the proportion of triggered charts that had an adverse event in INAES was 30% (211/703). This was different in the Utah/Colorado study which had a much lower adverse event rate (3%) and a much lower proportion of triggered charts (19.5%). (27)

There were subtle differences in the way preventability was defined between studies. The first study to address preventability was by Bates and colleagues who judged events as “probably or definitely preventable using current technology” (not further defined). (18) The Harvard Medical Practice Study did not assess preventability. It instead examined negligence as the purpose of the study was to assess the need and impact of a state wide malpractice insurance. The authors defined negligence as “failure to meet the standard of care reasonably expected of an average physician qualified to take care of the patient in question.” (11) However, most studies followed similar lines in that preventability was judged on the standards of care operating at the time. (28, 40, 45, 125).
In its definition of disability and adverse events, INAES included only physical harm, death and prolonged hospitalisation. This is consistent with the Canadian Adverse Events Study.(16) This stems from the original Harvard Medical Practice Study whereby a focus on eliciting negligent events required those with ‘measurable disability’ to be identified.(11) Therefore, the INAES estimates do not include psychological impacts or delayed discharge without injury. In contrast the Australian and Utah/Colorado studies did include mental distress.(27, 30) The INAES physician reviewers, however, did identify 15 (1%) admissions with delayed discharge or prolonged hospitalisation without physical injury which were not included in the adverse event rate. The French prospective study included psychological distress (from delays in treatment, lack of information, poor pain monitoring procedures) and this category had the highest proportion of preventable events (80%)(21)

5.9 INAES strengths

5.9.1 Comparability
The INAES data adds to international incidence and prevalence data on the burden of adverse events in acute hospitals. Within the constraints already discussed there is the ability to compare INAES with other large retrospective chart review studies and, in particular, the Canadian Adverse Events Study on which the data collection and protocol was based.(16) In addition, the systematic review provided the various criteria to recalculate our main results using different timing and location criteria for adverse event eligibility. This meant that within the limits of documentation in the index hospital, inclusion of outside the index hospital adverse events was possible. Such events add to the adverse event burden (and cost) for each hospital.
5.9.2 Sensitivity of the trigger methodology

The assessment of sensitivity and the high sensitivity for the stage-one screening to detect adverse events of INAES are strengths of the study. The two-stage methodology meant that not all charts undergo physician review - this increases review efficiency but raises the possibility of missing adverse events. To assess this, a sensitivity analysis of the trigger screening was conducted. This indicated that the adverse event rate would only increase by 4% (absolute increase 0.4%) to 12.7% if physicians had reviewed all study charts. Only four other chart review studies assessed their own sensitivity and specificity and the INAES figures (sensitivity 95.9%, specificity 64%) are in line with their results, e.g. Harvard Medical Practice Study(2): sensitivity 89%, the Brigham and Women’s Hospital study(18): sensitivity 93%, specificity 42%, Australian study(30): sensitivity 97.6%, specificity 67.3%, and the British study by Sari and colleagues(23): sensitivity 92%, specificity 62%.

5.9.3 Reviewers

The INAES employed experienced clinical reviewers (nurses and physicians) who received standardised training in the methodology. In addition, one of the research nurses had previous experience of chart review, one of the physicians had experience in review of adverse drug reactions and another in malpractice assessments. A further consideration for stage-two reviewers was whether they had worked at the hospitals under review. The advantage of internal reviewers is that they have “inside” knowledge about the care in that hospital but this could also affect judgements of causality and preventability.(143, 170) In the INAES, the physician reviewers were external to the INAES hospital sites, with the exception of one, who had knowledge of one of the sites on a visiting basis. This strengthened the independence of the assessments of causality and preventability.
5.9.4 Data collection tool
The data collection tool employed structured implicit review to aid judgements of causation by healthcare management and preventability in stage-two of the chart review. An explicit list of all adverse events is not possible so the judgement of these factors is implicitly based on the adverse event definition. However, the INAES data collection tool guided reviewers to an informed professional judgement. A series of questions prior to the six-point scales for causation and preventability were designed to assist reviewers to interrogate the patient's chart in a systematic and structured way. The database was also able to automatically determine whether an injury satisfied the INAES definition of an adverse event, and in those cases reviewers were asked for more details about the event. Thus, the tool provided a standard structured method to aid physician judgement and reviewer consistency and is a strength of the study.

5.9.5 Electronic random selection from HIPE discharge database
A further strength of the study was the ability to generate a random selection of in-patient data from the local HIPE databases. The nurse reviewers assessed whether the eligibility criteria of hospital stay over 24 hours was met from the information in the chart because the HIPE admissions data did not include times of admission or discharge. Nurse assessment is likely to be more accurate than HIPE data in assessing the length of hospital stay in cases where there is a delay between presentation (start of a hospital “stay”) and the admission documentation being complete. This nurse assessment to ensure appropriate application of this inclusion criterion is another strength of the study.

5.9.6 Dataset of adverse events
The use of stratification in INAES, of patients who were likely to have had surgery and those who did not undergo surgery, allowed an increased number of events to be analysed. This strengthens the depth of analysis possible of the adverse events. However, by doing this the sample was not
representative of acute adult hospital admissions in the Republic of Ireland. For this reason, the statistical analysis was weighted to revert to the INAES hospitals’ underlying configuration. Despite this, weighting had only a small effect on the results.

5.10 INAES limitations

5.10.1 Selection bias

It is possible that there was selection bias in INAES due to differences between the hospitals that agreed to participate and those that did not agree. Sixty percent of invited hospitals agreed to participate (n=18), six refused and six did not reply despite repeated email and telephone follow-ups. Hospitals did not provide a reason for non-participation but reasons could have included resourcing issues (medical records, space for the review) as well as the hospital’s patient safety culture, although this is speculative. Of note, two chart review studies of surgical mortality had recently been performed in a number of Irish hospitals and this may have influenced the decision to participate in INAES.(64, 159) However, the demographics (age, sex and length of stay) of the INAES population were similar to that of adult admissions to all Irish acute public hospitals and the INAES hospitals were stratified by size and region to ensure inclusion of an even mix of hospital types in the country. Therefore, we do not have evidence of any systematic differences between participating and non-participating hospitals.

It is possible with oversampling that charts not looked at, or missing, contained a different rate of adverse events. Nurses were instructed to review from the oversample only when the initial list of 100 “surgery” and 100 “non-surgery” charts had been exhausted. The Harvard Medical Practice Study was able to check missing charts for adverse events after data collection was complete for the main study and they found a lower rate of events in these charts (2.5% compared with 4.2%).(2) Whilst this data
provides reassurance that missing charts are unlikely to significantly inflate the adverse event rate, it cannot be assumed to apply to INAES.

5.10.2 Information bias

Retrospective chart review is restricted to documentation of information in charts without additional information from staff providing the patient care at the time of the adverse event. This may underestimate the adverse event rate. For example, studies comparing prospective and retrospective methodologies have found that although these methods identify similar rates of events, they do not necessarily identify the same adverse events. (125) Therefore the “true” adverse event rate will be the total events found by both methods. Prospective methods have also been found to be better at eliciting preventability. (22, 125) Therefore, the INAES preventability assessment, although high, may have been different if collected prospectively.

Reviewers were instructed to examine the chart centring on the index admission but also reviewing information a year before and after. Thus events occurring prior to this time period or detected afterwards will not be included. The Australian study estimated that 10% of their events occurred over a year prior to the index admission. (30) Thus, the INAES figures may slightly underestimate the true prevalence of admissions associated with adverse events.

One reason for retrospective chart review not capturing all adverse events could be that deficiencies in the chart mean that charts do not reflect the clinical scenario fully. (22) Charts may not provide insight into specific causes of adverse events. For example, if the chart demonstrates a lack of follow-up it may be because there was no appointment sent or because the patient did not come to an arranged follow-up clinic visit. (11) Hospital charts are also restricted to one hospital and adverse events that did not result in subsequent hospital admissions or out-patient visits at the index hospital will
not have been included, e.g. events detected in other settings or that are not detected.

Several studies have examined completeness of documentation as a way of assessing information bias and validity of the methodology. The New Zealand study found that 95% of patient charts contained sufficient information to enable all parts of the stage-one screening form to be completed. For the stage-two form this was 85%. However, this study reported that in all cases there was adequate information to be able to determine the presence of an adverse event.\(^{(43)}\) The Australian study found that half of charts were missing one or more elements and the proportion of admissions with adverse events was highest in charts with no missing elements, declining progressively with more missing sections. The authors concluded that missing documentation will mean that adverse events are less likely to be detected.\(^{(30)}\) However, this seemed to have a relative small effect - in their study only 0.4% of charts contained an adverse event that was strongly suspected by physicians but there was insufficient evidence or documentation in the chart to confirm this. The British study by Vincent and colleagues found that half of records were reasonably clear and well-structured but in the other half there were deficits including missing reports, inadequate discharge summaries, insufficient clinical notes, lack of initial medical assessment, insufficient clinical progress notes, or missing procedure documentation. Over a third were so poorly organised, it was difficult to extract information.\(^{(137)}\)

In INAES, if a chart had insufficient documentation to determine the presence of a trigger it was considered ineligible and not reviewed. For eligible charts, nurse reviewers collected information on the documentation status of each record. This data could be further analysed according to the relationship of inadequacies in the documentation (type and extent) and eventual adverse event determination. The INAES physician reviewers also commented that there was significant variability across hospitals in terms of
filing practices, recording of information (extent of documentation, handwritten or typed), layout of drug charts, presence of discharge summaries, and availability of investigation results.

It may be that some adverse events are better identified through retrospective chart review than others. For example, those related to surgery may be easier to identify due to more consistent documentation than other types of adverse events. (33) This should be considered when reviewing the events for their root cause. Another consideration is that human actions are reported on a patient record and therefore human causes will be the most visible. In contrast, technical and organisational factors are less likely to be well recorded, although they may have been significant contributing factors to the adverse event. (143)

5.10.3 Hindsight or outcome bias
There is the possibility of overestimation of adverse events through hindsight or outcome bias especially if the factors influencing clinical decision making are not well documented. (33) Knowing the outcome of an event may influence a reviewer in his/her judgements of causality and preventability. To reduce this bias the INAES employed standardised training for reviewers and structured data collection. Prior to determining causation or preventability using the six-point scale, reviewers progressed through a series of events designed to make the reviewer consider an explicit list of other factors that may be relevant to the decision.

Hindsight bias is a particular issue with the assessment of death due to adverse events and preventability. Retrospective record review for adverse events has been shown to overestimate the proportion of preventable deaths due to adverse events. (170, 171) A British representative review of hospital deaths found that 13% had a problem in care that contributed to the death and 40% of these were judged to be preventable (equivalent to 5% of all
hospital deaths).(172) The INAES did not collect information on probability of death or life expectancy without the adverse event, in admissions where the person suffered an adverse event and died. Therefore, conclusions around whether an event caused the death are problematic. The Dutch studies specifically included half of their samples as deceased and designed data collection to include additional variables around these issues.(15, 31, 126) Without this, the INAES is only able to say that the event may have resulted in, or contributed to, death - no direct causation link should be made. This limitation is also true when assessing the association between preventability and death. Preventability of an adverse event should not be extrapolated to preventability of the associated death.(30, 173) Additional information on the INAES adverse event associated deaths may be obtainable through review of the physician and nurse clinical summaries and re-analysis. This has been performed by other similar adverse events studies.(137, 173) An advantage of the Harvard Medical Practice Study methodology is that, because unexpected death is a trigger, physicians will have reviewed all such cases and, therefore, such additional analysis of all the deaths could be performed.

Other studies have collected more information in relation to the deaths. The studies by Vincent and colleagues in the UK and the Spanish study conducted by Aranaz-Andres and colleagues instructed the reviewers to specify the relationship of the death to the adverse event using three criteria (death unrelated to the event, death resulting from the hospital stay, death entirely due to the event).(14, 28) For future adverse event studies, inclusion of questions about life expectancy and the relationship of death to the adverse event in the INAES web-based data collection tool should be considered.
5.10.4 Reviewer bias

Consistency between reviewers is a challenge for all chart review studies and standardised reviewer training and computerised data entry have been recommended as ways to increase this.\(^{16}\) Consistency between reviewers (inter-rater reliability) is assessed via calculation of the kappa statistic. The INAES kappa value for nurse reviewers (stage-one) was 0.78 and for physicians (stage-two) was 0.59. These compare well with other adverse event studies where stage-one kappas ranged from 0.53\(^{33}\) to 1\(^{34}\) (mean 0.69) and stage-two kappas ranged from 0.25\(^{31}\) to 0.86 \(^{21, 125}\) (mean 0.63).

Stage-one review for triggers uses an explicit list of triggers and therefore kappa values tend to be higher than for stage-two. In contrast, stage-two involves implicit judgement (by experienced physicians) as it is not possible to have an explicit list of every type of adverse event.\(^{11}\) Furthermore, in order for reviewers to agree that an adverse event has occurred, all three elements of the definition (injury, resulting disability at discharge/ prolonged hospitalisation/ death, and causation) must concur. To enhance consistency the Irish National Adverse Events Study followed other studies in their use of structured data collection, standardised group training and employed experienced physicians.\(^{16, 20}\) However, some variability in judgement may exist due to each reviewer having unique clinical experiences and training. One study looking at preventability in hospital deaths found skewed preventability judgements among reviewers and concluded that if several reviewers evaluated a chart there would always be some who believe strongly that death could have been avoided.\(^{170}\)

The physician reviewers in INAES were general physicians and there were no surgeon reviewers. A surgical collaborator was available to answer questions and reviewers were encouraged to discuss difficult cases with the other reviewers and/or the principal investigator and/or the surgical collaborator. The Harvard Medical Practice Study also used generalists
(physicians and surgeons). In their pilot study, they found that internists and surgeons could identify adverse events with a high degree of accuracy. They commented that it was not feasible to have a specialist in the appropriate field to review each adverse event.(174) In addition, many adverse events - although they may occur in a specialty setting - will be of a general nature, e.g. post-operative pneumonia, antibiotic-associated diarrhoea. However, the challenge remained for our reviewers to assess causation and preventability in technical settings because this required knowledge of applicable practice standards at that time and accepted rates of complications of specialist surgery, e.g. orthopaedics.

5.10.5 Harvard methodology and Canadian data collection tool
Although the Harvard Medical Practice Study methodology is considered the gold standard, it is unclear whether the healthcare management and preventability scales used have been validated. There are also differences between studies purporting to use the same method. For example, the six-point causation scale was not consistent across studies. The forms used by the British study by Vincent and colleagues grade causation by healthcare management in terms of probability (virtually no evidence, minimal probability, slight probability, moderate probability, highly probable evidence for management causation, virtually certain evidence for management causation) rather than the 50:50 grading used in INAES and the Canadian Adverse Events Study.(13, 14, 16, 28)

The Irish National Adverse Events Study employed the Canadian Adverse Events Study methodology and data collection tool. This restricted data analysis to particular adverse event groupings. Healthcare-associated infection was not included as a category of event on its own but was captured under surgical and medical procedures and free text in other categories. The Canadian study was based on the original Harvard Medical Practice Study and was published in 2004. Given the rise in interest and
frequency of healthcare-associated infections this part of the web-based data collection tool should be re-categorised for future use.

5.11 Impacts of this thesis

The actual and potential impacts of the work in this thesis are discussed below using the framework by Kuruvilla and colleagues. (175)

5.11.1 Research-related impacts

The findings from this thesis have significant research-related impacts. This work provides the first national data on adverse event frequency in adult in-patients of acute hospitals in the Republic of Ireland. The results provide a baseline figure for Ireland against which further assessments of adverse event rates can be compared. The application of the Harvard Medical Practice Study trigger methodology in the Irish hospital setting ensures international comparability of INAES findings. It will enable replication of the study using the Harvard definition of an adverse event and methodology for future studies in the area. The systematic review updated knowledge in this area and demonstrated the lack of data on patient risk factors for adverse events and the methodological differences between frequently compared international adverse event studies.

The background work from this thesis has been published as a review article in the *QJM*, a journal for hospital physicians (impact factor 2.495), and as a poster for the Irish National Patient Safety conference held in Dublin in November 2014. The INAES main results paper is currently under review at the *BMJ Quality & Safety* journal, a leading journal in the field (impact factor 3.988). A poster abstract of the main results has also been submitted to the International Forum on Quality and Safety in Healthcare for display in April 2016, Sweden. A poster of the patient characteristics results of the systematic review will be presented at the RCSI research day and a paper has been written. The methodology results of the systematic review will also
be drafted into a paper. This research has enabled me to submit this thesis. It has also offered a medical student the opportunity to be involved in a research project.

The web-based data collection tool has been adapted to the Irish setting. It will be handed over to the HSE and made available to all public hospitals in the Republic of Ireland for local and national patient chart review studies.

The INAES has established a patient safety research network through the membership of the working and advisory groups: consisting of clinicians, healthcare policy makers and experts in patient safety, human factors, health systems, and quality. These research groups will be maintained for dissemination of the INAES results, future analyses on the dataset and development of a patient safety research agenda for Ireland. In addition, the INAES was the demonstrator project for the Research Collaborative in Quality and Patient Safety, a unique initiative in Ireland involving the national health research funding agency (the Health Research Board), the HSE and the Royal College of Physicians of Ireland.

Ongoing dissemination of this work will include peer reviewed publication of the INAES results with media statements to coincide with publication of the main results (and prior briefing of key policy makers), posters and presentations at national and international patient safety related conferences. Target audiences for this research include: quality and risk personnel, senior management teams in hospitals and clinics, practising physicians, nurses, allied health professionals, healthcare managers, primary care professionals, nursing homes, patients and patient safety groups, professional training bodies, Health Research Board, and health media.
5.11.2 Policy-related impacts
The findings of this thesis are likely to have significant policy impacts. It is expected that the results of INAES will influence patient safety policy at national and local levels. Furthermore, the Department of Health is currently restructuring its patient safety department and the results of INAES will be timely. The nature of the influence on healthcare policy of the INAES results will be both instrumental and provide supportive evidence to drive policy. Policy briefs derived from INAES findings will provide evidence to support ongoing and proposed policy activities, and also raise awareness and support for new policy making in the field of patient safety. It is hoped that funding will be obtained to develop a policy network through a series of policy dialogues.

A significant output of the INAES work will be development of a policy brief regarding the frequency and nature of adverse events in Ireland and the implications of the findings of INAES. This will be forwarded to national agencies such as the Department of Health, the HSE, HIQA, Directors of the Clinical Programmes, National Clinical Effectiveness Committee, all hospital Chief Executive Officers, hospital Clinical Directors and Directors of Nursing, and others as appropriate.

5.11.3 Service-related impacts
The INAES has the potential to influence health services management by raising the profile of patient safety. The INAES estimation of the financial cost of adverse events, along with the obvious human cost of these events, should act as major drivers of patient safety initiatives in local healthcare organisations and national policy fora. By raising the profile of patient safety in Ireland it is anticipated that publication of the INAES findings will help the implementation of quality guidelines and patient safety policy. The findings of INAES will draw attention to deficiencies in the healthcare system in relation to patient safety initiatives, such as inadequate resourcing and staff training, and to the potential to develop targeted interventions to address behaviours
(staff and patient) that will serve to reduce the occurrence of adverse events in Ireland.

The web-based tool used in INAES will enable healthcare services in Ireland to conduct their own chart review studies on an ongoing basis. I will work with the HSE to adapt the tool further for this use and provide staff training. Four local nurses have been trained in the methodology and could be involved in local implementation of the tool. The HSE and Department of Health are developing the health service information technology infrastructure in Ireland, with an electronic health record and unique health identifiers pilot underway. It is possible that the INAES data collection tool could also be incorporated in some way into this development allowing identification of those at greater risk of adverse events on an ongoing basis.

5.11.4 Societal-related impacts
The findings of this thesis are likely to have societal importance. Dissemination of the INAES results could lead to changes in knowledge about patient safety by patients and families, healthcare workers and managers. However, publicity and dissemination of the study findings are key and should avoid stigmatising healthcare organisations and staff. Instead, awareness should be raised about the second victims of adverse events, namely the healthcare workers. The presence of Irish data may influence healthcare professionals' behaviour towards patient safety initiatives. Media attention may increase health literacy of both healthcare professionals and the general population in relation to patient safety.

The INAES findings could also be used to develop social capital and community empowerment in patient safety. The resulting openness about patient safety could be used to engender trust and replace the suspicion of the current investigative and punitive approaches to patient safety.
In the long term, improvements in patient safety through raised awareness and policy could result in a reduction in adverse events which will beneficially impact on patients, the workforce and society. The findings from INAES should be part of a sustainable development approach to our healthcare system – influencing a healthy and just society, using sound science responsibly, and promoting good governance.

5.12 Future analyses
The year 2009 was chosen as it pre-dated the establishment of the National Clinical Care Programmes in Ireland, which aimed to improve and standardise the quality of patient care. INAES provides important baseline data enabling future evaluation of the effect of these programmes on patient safety. The study could therefore be repeated using 2015 patient charts to show trends in the prevalence and nature of adverse events in the six years since implementation of the Clinical Programmes.

Each INAES adverse event category includes a range of event sub-categories. For example, operation-related adverse events included wound infections, technical complications like bleeding or failure of wound closure, nontechnical complications such as pulmonary embolism, surgical failure, and delayed complications. Further research with the INAES data could examine the sub-categories within these broad clinical areas and evaluate their frequency, impact, and preventability. This will assist healthcare providers and policy makers in prioritisation of future patient safety initiatives. For example, some types of events may be more preventable or have greater impact and these factors may direct policy makers to areas of priority for intervention. In the Harvard Medical Practice Study the highest rates of serious disability were found for diagnostic (47%) events whereas the lowest were for technical operative complications (12%) and drug related events (14%). Ideally interventions and further studies should focus on types of events with high preventability and high impact (and high cost). For example diagnostic errors are associated with high preventability and potentially high
impact. A missed diagnosis resulting in presentation at a later stage can result in large downstream costs.(176) A subsequent analysis of INAES data could also look at distribution of preventable in-hospital events in terms of hospital or out-of-hospital location and healthcare provider.

Additional analysis of the INAES data could also examine whether age was an independent predictor after adjustment for co-morbidity. This could include examining whether the nature (type, impact and preventability) of adverse events change with increasing age.

Future analyses of the INAES data could also elicit the relationship between preventability and severity of the adverse event. This has varied across studies which reported this data. The Spanish and Canadian studies did not find a relationship between preventability and severity.(14) The Australian study, on the other hand, found a higher proportion of preventability with events with a more severe impact (death or above 50% permanent disability): preventability was 70% in this group compared with 51% overall.(30)

Additional work could examine whether any differences exist between patients (who have undergone surgery or have not, or by specialty) regarding the severity of the adverse events and their preventability. The New Zealand study found surgical events were less severe with a lower proportion of deaths, and a lower proportion were preventable, compared with medical events.(39)

Further analysis of the INAES data could compare events which occurred prior to the index hospitalisation with events which occurred during the admission for differences in frequency, impact and preventability. The New Zealand study found that pre-hospital events resulted in longer attributable
bed days (8.4 versus 4.5 days) and events which occurred outside the index hospital (e.g. in ambulatory care) resulted in more bed days than those associated with index hospital admissions (8.0 versus 6.1 days). (39)

Other potential analyses of the INAES data include:

- Analyse primary care events
- Review the nurse reviewer assessment of chart documentation and its relationship with subsequent adverse event determination
- Logistic regression of patient characteristics to build a patient profile of adverse event risk
- Compare HIPE diagnoses with nurse reviewer extracted co-morbidity data.
- Analysis of adverse event rates by diagnosis related groups (DRGs) and Charlson Index of morbidity to assess diagnosis-treatment complexity relationship with adverse event risk
- Re-analyse clinical summaries of adverse events contributing to death in light of the life expectancy of the patient if the adverse event had not occurred
- Re-analyse clinical summaries for a more detailed cost analysis – additional procedures performed, transfers to a higher dependency bed

A qualitative analysis of the adverse events, including quality assessment methods such as root cause analysis, could be performed and linked to intervention recommendations. (30). The Dutch have published a paper focussing on causes (latent conditions and active errors) of their adverse events using Reason’s theoretical framework and linked these to prevention strategies. (143) Within this work, the role of patients in adverse events could be investigated. The original adverse events study in Californian hospital in-patients, which led to the Harvard Medical Practice Study, found patients
were responsible for events at a rate of 0.4%, especially in the areas of self-management of diseases and failure to follow medical advice.(120)

The INAES results describe the burden of adverse events in Ireland. Nevertheless, the retrospective methodology may be viewed as a blunt instrument for monitoring specific quality initiatives.(107) This is because adverse events represent a heterogeneous group, e.g. medication-related and peri-operative events.(107) A reduction in one category may be counter-balanced by an increase in others, leading to no overall change in adverse event rates. Thus interventions to reduce adverse events need to be targeted at specific adverse event categories, and future studies monitoring effects tailored accordingly.(107, 167) These studies could be performed by local hospital or national groups as the web-based tool adapted for INAES provides an electronic application for chart review and will allow hospitals to conduct their own reviews and monitor their implementation of patient safety initiatives.
5.13 Summary of the INAES results and recommendations

5.13.1 Summary of the INAES results

- Adverse event prevalence 12.2%.
- 72.7% of events were judged to be preventable.
- Adverse event incidence density of 10.3 adverse events per 100 admissions.
- Impact: Over two-thirds of adverse events resulted in no or minor impairment, 9.9% were associated with permanent impairment, 6.7% were associated with death.
- Hospital readmission and prolonged hospital stay were the most frequent healthcare outcomes of adverse events.
- Adverse event risk was highest in those who had procedure codes indicating surgery was likely to have been performed. However, when the data was analysed according to the specialty code of the principal diagnosis, there was no difference in risk between medical and surgical specialties.
- The most common event category was operation-related events; followed by therapeutic-related, medication-related or diagnostic events.
- Increasing age, but not sex or type of admission (elective or emergency), was associated with a greater risk of an adverse event.
- Each adverse event resulted in an additional 6.1 days and €5550 cost, extrapolating to €194 million nationally in 2009.
5.13.2 Recommendations

1. Dissemination of this work to the healthcare sector (policy makers, service delivery, international community) and research funders:
   a. to policy makers and research funders by publication of main INAES results in BMJ Quality and Safety with an associated press release and pre-publication briefing of key organisations (HSE, Department of Health, HIQA, Health Research Board, Royal College of Surgeons in Ireland and Royal College of Physicians of Ireland);
   b. to the healthcare sector service delivery via a report of the main results of INAES provided to the HSE and Department of Health. The web based data collection tool will also be made available to the HSE for use in the sector;
   c. to the international quality and patient safety community by publication of the main results of INAES in BMJ Quality and Safety and a poster at the International Forum on Quality & Safety in Healthcare.

2. Future research using the INAES methodology and patient safety research network should include:
   a. additional analyses of the existing INAES dataset examining in more detail the event types, severity, preventability and risk factors;
   b. repeating the study (in full or part) using more recent admissions to show trends in adverse events after implementation of the National Clinical Programmes;
   c. working with the healthcare sector to adapt the web based data collection tool for use by hospitals for local and national patient chart review studies.
3. Utilisation of the INAES methodology and results by the healthcare sector should involve:
   a. the HSE making the INAES patient chart review methodology available for use in hospitals for local patient chart review studies (including adapting the web based data collection tool for independent use by hospitals and providing training and support to hospital staff);
   b. the HSE and CIS reviewing the current NIMS voluntary reporting rates and patterns in light of the INAES results;
   c. engagement by the INAES research team with the HSE and Department of Health regarding specific areas of risk which have not been addressed by the National Clinical Programmes and other quality initiatives post 2009.
5.14 Conclusion
The Irish National Adverse Events Study is the first national study to report rates of adverse events in the Irish acute adult hospital setting. It provides an important measure of the burden and impact of events - in terms of morbidity, mortality and cost. The major strength of this research is its standardised definition and methodology to establish the national frequency of adverse events. Whilst the study was conducted in the Irish healthcare system, many of the findings will be generalisable to other settings and the results add to the existing international literature in the field.

The INAES employed web-based electronic data capture which has the potential to make the methodology more accessible for organisations to assess and monitor their patient safety initiatives on an ongoing basis. As Irish healthcare has undergone extensive change due to the economic recession and the growth of the quality movement, this study of adverse events in 2009, near the start of these dual influences, provides an important baseline and the opportunity to link safety with subsequent organisational reform.

The results give an overview of the types of patient safety issues which will help guide future interventions to reduce specific adverse events and improve safety in the Irish healthcare setting. Discrepancies between the INAES rate of adverse events and that reported to the national incident reporting system highlight the important need to encourage the development of a “no-blame” culture in healthcare in Ireland, thus maximising a “reporting culture”, where adverse events and near misses can be addressed in a timely and transparent manner, for the benefit of patient outcomes and staff well-being.

To err is humane; to forgive, divine.
Alexander Pope, An Essay on Criticism, 1711, London
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Appendices

Appendix 1: Clinical Indemnity Scheme Notification Report Form

Sample Adverse Event Notification Form

Clinical Indemnity Scheme Notification Report Form: NAEMS Ref No. _____________

Location ___________________________ Clinical Area/Unit/Department ___________________________

Date of occurrence (dd/mm/yyyy) ___/___/___ Time of occurrence (24hrs) ___:___ hrs

Date event reported (dd/mm/yyyy) ___/___/___

Service User/Patient Personal Details: ID No.

Name __________________________ D.O.B. (dd/mm/yyyy) ___/___/___ Gender M [ ] F [ ]

Patient Safety Incident / Adverse Event [ ] Near Miss [ ]

Was the Service User Actually Harmened? Yes [ ] No [ ] Not yet known [ ]

Describe the harm sustained including patient outcome:

____________________________________________________________________________________

____________________________________________________________________________________

Did any actions prevent the incident from reaching the service user? Yes [ ] No [ ] Not yet established [ ]

Describe the preventative actions taken:

____________________________________________________________________________________

____________________________________________________________________________________

Incident Type ______________________ (see NAEMS pick list)

Brief Description of Incident:

____________________________________________________________________________________

____________________________________________________________________________________

Specialty involved? ______________________ Sub-specialty? ______________________ (see NAEMS pick list)

Risk Analysis Matrix – based on current available information; may be amended upon receipt of additional information.

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Negligible (1)</th>
<th>Minor (2)</th>
<th>Moderate (3)</th>
<th>Major (4)</th>
<th>Extreme (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almost certain (5)</td>
<td>10</td>
<td>9</td>
<td>8</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Likely (4)</td>
<td>4</td>
<td>8</td>
<td>12</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Possible (3)</td>
<td>3</td>
<td>6</td>
<td>9</td>
<td>12</td>
<td>15</td>
</tr>
<tr>
<td>Unlikely (2)</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Rare/unique (1)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

Contributory Factor(s): (See list)

Primary: ______________________

Secondary: ______________________

Low Risk 1 – 5 Moderate Risk 6 – 12 High Risk 13 – 25

Reported by: Name: ______________________ (print) Title: ______________________ Signature: ______________________

Reported to: Name: ______________________ (print) Title: ______________________ Signature: ______________________

Reviewed by: Name: ______________________ (print) Title: ______________________ Signature: ______________________

Date Received in RM Office: _____/___/_____ Date Logged onto NAEMS: _____/___/_____
Appendix 2: HSE Safety Incident Management Policy List of Serious Reportable Events

HSE Safety Incident Management Policy 2014
Appendix 5: List of Serious Reportable Events

1. SURGICAL EVENTS
A. Surgery performed on the wrong body part by a healthcare provider
B. Surgery performed on the wrong patient by a healthcare provider
C. Wrong surgical procedure performed on patient by a healthcare provider
D. Unintended retention of a foreign object in a patient after surgery or other procedure performed by a healthcare provider
E. Intra-operative or immediately post-operative death of a normal healthy patient with no known medical problems after surgery or other procedure performed by a healthcare provider

2. PRODUCT OR DEVICE EVENTS
A. Patient death or serious disability associated with the use of contaminated drugs, devices, or biologics provided by the healthcare provider.
B. Patient death or serious disability associated with the use or function of a device in patient care provided by the healthcare provider in which the device is used or functions other than as intended or anticipated.
C. Patient death or serious disability associated with intravascular air embolism that occurs while being cared for by a healthcare provider but excluding death or serious disability associated with neurosurgical procedures known to present a high risk of intravascular air embolism.

3. PATIENT PROTECTION EVENTS
A. Child or other dependent person discharged to the wrong person by a healthcare provider.
B. Patient death or serious disability associated with patient absconding from a healthcare facility whilst under medical supervision but excluding where the patient advises the healthcare provider that he or she is leaving against medical advice.
C. Patient suicide, or attempted suicide, resulting in serious injury or disability while receiving health services from a healthcare provider.

4. CARE MANAGEMENT EVENTS
A. Patient death or serious disability associated with a medication error by the healthcare provider but excluding reasonable differences in clinical judgment involving drug selection and dose.
B. Wrong route administration of chemotherapy by a healthcare provider.
C. Intravenous administration of mis-selected concentrated potassium chloride by a healthcare provider.
D. Patient death or serious disability associated with a haemolytic reaction due to the administration of incompatible blood or blood products by a healthcare provider.
E. Maternal death or serious disability, occurring within 42 days post-delivery, associated with labour or delivery in any pregnancy while being cared for by a healthcare provider.
F. Death or serious injury of a neonate associated with labour or delivery in a low-risk pregnancy.
G. Patient death or serious disability associated with hypoglycaemia, the onset of which occurs while the patient is being cared for in a healthcare facility.
H. Death or serious disability (kernicterus) associated with failure by a healthcare provider to identify and treat Hyperbilirubinaemia in infants within the first 28 days of life.
I. Stage 3 or 4 pressure ulcers acquired after admission to a healthcare facility but excluding progression from Stage 2 to Stage 3, if Stage 2 was recognised upon admission.
J. Patient death or serious disability due to spinal manipulative therapy by a healthcare provider.
K. Artificial insemination with the wrong donor sperm or wrong egg by a healthcare provider.
5. ENVIRONMENTAL EVENTS
A. Patient death or serious disability associated with an electric shock while being cared for in a healthcare facility but excluding events involving planned treatments such as electric counter shock or elective cardioversion.
B. An incident in which a line designated for oxygen or other gas to be delivered to a patient while being cared for by a healthcare provider contains the wrong gas or is contaminated by toxic substances.
C. Patient death or serious disability associated with a burn incurred within a healthcare facility.
D. Patient death or serious disability associated with a fall while being cared for in a healthcare facility.
E. Patient death or serious disability associated with the use of physical restraints or bedrails while being cared for in a healthcare facility.

6. CRIMINAL EVENTS
A. Any instance of care ordered by or provided by someone impersonating a healthcare professional.
B. Abduction of a patient of any age while being cared for in a healthcare facility.
C. Sexual assault on a patient within or on the grounds of a healthcare facility.
D. Death or serious injury of a patient or other person resulting from a physical assault that occurs within or on the grounds of a healthcare facility.
E. Patient death or serious disability associated with physical assault while being cared for in a healthcare facility.
Appendix 3: Systematic review database searches

Cochrane Central Register of Controlled Trials (Wiley InterScience)

The Cochrane Library 1980 to 2015, searched on 20 June 2015, 405 records retrieved

1. “Harvard medical practice”
2. “adverse event”
3. “adverse events”
4. preventable
5. “iatrogenic injury”
6. “iatrogenic injuries”
7. “medical error”
8. “medical errors”
9. #2 AND #4
10.#3 AND #4
11.#4 AND #5
12.#4 AND #6
13.#4 AND #7
14.#4 AND #8
15.”patient harm” [MeSH Terms]
16.”iatrogenic disease” [MeSH Terms]
17.#1 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16

MEDLINE (PubMed)

MEDLINE PubMed 1980 to 2015, searched on 20 June 2015, 1266 records retrieved

1. “Harvard medical practice”
2. “adverse event”
3. “adverse events”
4. preventable
5. “iatrogenic injury”
6. “iatrogenic injuries”
7. “medical error”
8. “medical errors”
9. #2 AND #4
10.#3 AND #4
11.#4 AND #5
12.#4 AND #6
13.#4 AND #7
14.#4 AND #8
15.”patient harm” [MeSH Terms]
16.”iatrogenic disease/complications” [MeSH Terms]
17.#1 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
EMBASE (Ovid SP)

EMBASE 1980 to 2015, searched on 20 June 2015, 3220 records retrieved

1. ‘Harvard medical practice’
2. ‘adverse event’
3. ‘adverse events’
4. ‘iatrogenic injuries’
5. ‘iatrogenic injury’
6. ‘medical errors’
7. ‘medical error’
8. preventable
9. ‘patient harm’
10. ‘iatrogenesis’/exp
11. #2 AND #8
12. #3 AND #8
13. #4 AND #8
14. #5 AND #8
15. #6 AND #8
16. #7 AND #8
17. #1 OR #9 OR #10 #11 OR #12 OR #13 OR #14 OR #15 OR #16

PsycINFO (Ovid SP)

PsycINFO 1967 to 2015, searched on 20 June 2015, 255 records retrieved

1. “Harvard medical practice”
2. “adverse event”
3. “adverse events”
4. “iatrogenic injuries”
5. “iatrogenic injury”
6. “medical error”
7. “medical errors”
8. “patient harm”
9. “iatrogenic disease”
10. preventable
11. 2 and 10
12. 3 and 10
13. 4 and 10
14. 5 and 10
15. 6 and 10
16. 7 and 10
17. 1 or 8 or 9 or 11 or 12 or 13 or 14 or 15 or 16
CINAHL (National Health Service Health Information Resources)

CINAHL 1982 to 2015, searched on 20 June 2015, 1111 records retrieved

1. “harvard medical practice”
2. “adverse event”
3. “adverse events”
4. preventable
5. “iatrogenic injury”
6. “iatrogenic injuries”
7. “medical error”
8. “medical errors”
9. “patient harm”
10. (MH”iatrogenic disease/CO”)
11. #2 AND #4
12. #3 AND #4
13. #4 AND #5
14. #4 AND #6
15. #4 AND #7
16. #4 AND #8
17. #1 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
Appendix 4 Systematic review data extraction tables

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<tbody>
<tr>
<td>Population</td>
<td>New York</td>
<td>Boston</td>
<td>NSW and S Australia</td>
<td>Utah and Colorado</td>
<td>Greater London</td>
<td>Auckland</td>
<td>New Zealand</td>
<td>Ottawa</td>
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<tr>
<td>Hospitals</td>
<td>51, non-federal acute care hospitals, stratified (teaching, ownership)</td>
<td>1, acute hospital</td>
<td>28, randomly selected, public and private acute care hospitals</td>
<td>28, included private hospitals, exclude hospitals that exclusively provide psychiatric, rehabilitation, drug/alcohol services (and Vets Admin Hospitals), stratified by size, location, teaching, ownership</td>
<td>2, acute hospitals</td>
<td>3 public hospitals Auckland region</td>
<td>13, random sample of 20 generalist public hospitals providing acute care &gt;100 beds, stratified by hospital type and geographical area</td>
<td>2, teaching hospitals</td>
</tr>
<tr>
<td>No. of records</td>
<td>30121 (30195)</td>
<td>3128 with complete screening data,(22) 3137(18)</td>
<td>14179</td>
<td>14700</td>
<td>1014 (pilot)</td>
<td>1575 (pilot)</td>
<td>6579</td>
<td>502</td>
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<tr>
<td>Method</td>
<td>HMPS (18 triggers adapted from California study(120)) + negligence (no preventability)</td>
<td>O’Neil: HMPS (15 triggers, no obstetric) vs. physician reporting, Bates: HMPS vs. billing screens data</td>
<td>HMPS (disability included impairment of mental function) (18 triggers) + preventability</td>
<td>HMPS (18 triggers, 2 different - temp&gt;38.3 day before discharge, injury/complication)</td>
<td>HMPS (own forms and scales)</td>
<td>HMPS (18 triggers=QAHC)</td>
<td>HMPS (18 triggers=QAHC)</td>
<td>HMPS (16 criteria QAHC but no inapprop d/c home/inadeq d/c plan, no readmission post index)</td>
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<td>on related to ambulatory surgery resulting in admission/ED presentation. No HAI, no documentation of dissatisfaction + expert review of all AEs to check met definition</td>
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<tr>
<td>Sampling</td>
<td>Random sample of non-psychiatric hospitalized patients, oversampled high risk low volume specialties, e.g., neurosurgery/vascular and complicated births, under sampled normal deliveries (numerous) and patients &gt;70 years (economic impact less variable)</td>
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<td>Patient population</td>
<td>All patients in non-psychiatric</td>
<td>All admissions to a medical</td>
<td>All patients excluding day</td>
<td>All patients excluding</td>
<td>General medicine,</td>
<td>All patient admissions</td>
<td>All patients excluding day,</td>
<td>Adults admitted for acute care of</td>
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<td>hospitals</td>
<td>service over 4 months</td>
<td>only admissions and admissions to designated psychiatric wards</td>
<td>psychiatric, drug and alcohol, and rehabilitation DRGs</td>
<td>general surgery, orthopaedics, obstetrics</td>
<td>excluding day and psychiatric</td>
<td>psychiatric and rehabilitation only cases</td>
<td>non-psychiatric illnesses over 1 year - 2 acute care facilities</td>
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<tr>
<td>Adverse event review period</td>
<td>Trigger for pre = readmission &lt;6 months (if &gt;65 years old), &lt;12 months (if &lt;65 years old)</td>
<td>Entire medical record</td>
<td>Trigger for pre = readmission &lt;6 months (if &gt;65 years old), &lt;12 months (if &lt;65 years old)</td>
<td>No limit. Assessed full medical records.</td>
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<td>Reviewers</td>
<td>Stage 1 - medical record analysts (students), stage 2 - senior medical residents from another hospital, preventability judged by blinded physician investigators (and compared with reviewer preventability), 1 reviewer per chart. Physician self-reporting arm used reporting by frontline staff as stage 1 plus</td>
<td>Stage 1 - RNs, Stage 2 = 2 physicians, stage 3 = if disagree then review jointly and discuss with third physician to obtain consensus. All specialists&gt;10 years’ experience, physicians and surgeons, obstetricians, anaesthetists</td>
<td>Stage - trained nurse. Stage 2 - one physician per case, preventability judged by two study investigators</td>
<td>Stage 1 - Research nurses. Stage 2 - Consultant physician, surgeons, obstetricians. One review only, except for difficult reviews - duplicate review and discussion.</td>
<td>Stage 1 - registered nurses, stage 2 – medical officers, plus physician expert reviewer (ER), 1 reviewer per chart.</td>
<td>Stage 1 - Trained registered nurses (RN), trained medical officers (MOs) plus expert reviewer - where RN and MO disagreed. One physician reviewer per chart.</td>
<td>Stage 1 nurse, stage 2 physician reviewers (two reviewed each chart). Descriptions of trig negative charts were reviewed by physician reviewer, if showed suspicion of AE then these charts were re-reviewed</td>
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<tr>
<td>Timing and location</td>
<td>AEs – occurred and discovered in index and occurred before index (in out-patient care or earlier hospitalisation) and first discovered in index. <em><strong>must have been discovered in index</strong></em> Did not include those caused in index but discovered after in the main calculation because wanted to calculate an incidence (=discovered during the index). Only included out of hospitals AEs that resulted in hospitalisation.</td>
<td>Pre- responsible for all or part of index (an ongoing reason for the index admission). Post – occur during detected after. Not explicit about restriction to in-hospital or could include out-of-hospital events but location of events includes doctor’s office 8.7%, nursing home 1.8% and responsible specialty family practice=6.4%, therefore assume out-of-hospital pre-events are included</td>
<td>Pre - cause of index or discovered during index. AE occurred and discovered during. None discovered post were included in incidence rate (?Included in analysis of events though).</td>
<td>Not stated in paper but forms imply pre events were collected</td>
<td>Pre – occur at any time before (in any care setting) but be detected during or the reason for the index.***AE related to/occurred during/the index admission. Post- occur during, detected on a subsequent admission. **AE could have occurred outside hospital (doctor’s rooms, home, NH, private hospital).</td>
<td>Included pre-hospital events as long as they were discovered in the index, could have occurred in ambulatory care (GP, patient’s home, nursing home). No post index.</td>
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<tr>
<td>Trigger positive</td>
<td>26%</td>
<td>62.3%</td>
<td>43.7%</td>
<td>19.5%</td>
<td>39.9%</td>
<td>32.6%</td>
<td>62.6%</td>
<td>62.2%</td>
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<td>Healthcare management</td>
<td>&gt;=4</td>
<td>&gt;=2</td>
<td>&gt;=4</td>
<td>&gt;=2</td>
<td>&gt;=2 (and &gt;=4)</td>
<td>&gt;=2 (and &gt;=4)</td>
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record review of reported charts.
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<tr>
<td>causation level</td>
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<td>% of admissions with ≥1 AE</td>
<td>4.2% all AEs – pre/index/post, incidence rate (no AEs discovered post discharge)=3.7% (95% CI 3.2-4.2) (28% of AEs due to negligence)</td>
<td>2.7% for retrospective record review, 4.3% for both methods,(22) 11% for retrospective record review ?? in Bates (18)</td>
<td>16.6% (95% CI 15.2-17.9%).</td>
<td>Incident rate (no post) = 3.2%, weighted=2.9%±0.2%</td>
<td>10.8%</td>
<td>10.7% (causation ≥4 = 102, 7.7%)</td>
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<td>12.7% (10.1-16.0)</td>
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<tr>
<td>Events per 100 admissions</td>
<td>Events per 100 discharges by age: 0-15 12.91, 16-44 25.84, 45-64 47.43, 65+ 58.85(11)</td>
<td>Counted only 1 AE per patient (most disabling or caused the longest additional LOS). 133 events</td>
<td>If &gt;1 AE then only the event that caused the most disability was analysed</td>
<td>11.7, 10.8% if include only those occurring during index</td>
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<tr>
<td>Preventable level</td>
<td>≥4</td>
<td>≥4 = high preventability, 2-3=low preventability</td>
<td></td>
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<td>&gt;=2 (and &gt;=4)</td>
<td>&gt;=2 (and &gt;=4)</td>
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<tr>
<td>% of preventable AEs</td>
<td>43.5%</td>
<td>51.2% (47.9-54.5%) (8.3% of admissions). For death and permanent impairment &gt;50% disability preventability =</td>
<td>Surgical adverse events 54% preventable(41)</td>
<td>47% of patients had preventable AEs or 48% of AEs were preventable.</td>
<td>38.6%</td>
<td>37.1% (&gt;=4), 61.6% (&gt;=2)</td>
<td>37.5% (24/502=4.8%)</td>
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<tr>
<td>Kappa stage 1</td>
<td>NPV 92%</td>
<td>0.67 (SE 0.02)</td>
<td>0.55, injury k=0.43, preventability k=0.33, disability/prolonged stay k=0.49</td>
<td>0.4</td>
<td>0.622</td>
<td>0.47</td>
<td>kappa given for stage 1 and 2 together - 0.5 (77% agreement)</td>
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<tr>
<td>Kappa stage 2</td>
<td>0.61</td>
<td>0.57 (preventability 0.30)</td>
<td>No effect of gender in multivariate analyses. (41) No stat sig difference. (74)</td>
<td>No stat sig difference</td>
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<tr>
<td>Sex</td>
<td>AE rates Female 3.7% Male 3.8%</td>
<td>No major differences (female 16%, male 17%). Preventability not strongly associated with sex. (30) Not stat sig. (36)</td>
<td>Patients with AEs were older than those who did not experience an AE (p&lt;0.001). Preventability increased with age: 0-14 3.3%, 15-29 4.9%, 30-44 6.5%, 45-65 7.8%, 65+ 8.1% (138) Preventable in hospital AEs increasing risk</td>
<td>No stat sig difference</td>
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<td>Age</td>
<td>Rates of AEs increased strongly with increasing age (p&lt;0.0001). Increased mean rate of AEs above 45 years. Persons 65 or older had more than double the risk of persons</td>
<td>Proportion of admissions associated with AEs increased with age&gt;30. Admissions resulting in more serious disability or death increased markedly with age. Preventable AE rates: 16-64 2.8% (preventable 1.58%), 65+ 5.29% (preventable 2.95%), stat sig. elderly had higher incidences of preventable AEs related to patients with AEs were older than those who did not experience an AE (p&lt;0.001). Preventability increased with age: 0-14 3.3%, 15-29 4.9%, 30-44 6.5%, 45-65 7.8%, 65+ 8.1% (138) Preventable in hospital AEs increasing risk</td>
<td>No stat sig difference</td>
<td>Increased with age 65+ (32) Preventability increased with age: 0-14 3.3%, 15-29 4.9%, 30-44 6.5%, 45-65 7.8%, 65+ 8.1% (138) Preventable in hospital AEs increasing risk</td>
<td>No stat sig difference</td>
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69.9% and 57.8%

Kappa given for stage 1 and 2 together - 0.5 (77% agreement)

Sex AE rates Female 3.7% Male 3.8%

No major differences (female 16%, male 17%). Preventability not strongly associated with sex. (30) Not stat sig. (36)

No effect of gender in multivariate analyses. (41) No stat sig difference. (74)

Patients with AEs were older than those who did not experience an AE (p<0.001). Preventability increased with age: 0-14 3.3%, 15-29 4.9%, 30-44 6.5%, 45-65 7.8%, 65+ 8.1% (138) Preventable in hospital AEs increasing risk

Risk of adverse events was significantly associated with age (p<0.001). <34 3%, 34-54 10%, 35-72 16%, >72 22%
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<tr>
<td>16-44yrs. AE mean standardised (for diagnosis) rates newborn 1.4, &lt;16 2.7, 16-44 2.6, 45-64 4.7, 65+ 5.9.</td>
<td>AEs were not strongly associated with age except increase in preventable AEs causing death for patients&gt;65. Proportion of admissions associated with permanent disability/death due to AEs increased with age. Temporary disability/prevent ability were not associated with age or other patient variables. Rates 0-14 10.8%, 15-29 10.3%, 30-44 14.6%, 45-64 19.3%, 65+ 23.3%.</td>
<td>medical procedures, ADEs, falls.(27) Increased risk of surgical AEs was assoc with older age (OR 5.0, CI 3.0-8.4, for age 64 years verses age&lt;15 years). After adjusting for patient and hospital characteristics, age was not an independent RF. Implies care more complex rather than age discrimination.(41)</td>
<td>with Age: 0-29 OR 1, 30-64 OR 1.8 (1.42-2.29), 65+ OR 2.43 (1.86-3.17)(139)</td>
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<td>In the elderly, 4 classes of AEs occurred ≥2x as often as in younger patients - nontechnical post op complications, non-invasive treatment mishaps, fractures and falls.</td>
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<td>13.4% (preventable 36%), 65+ 28.9% (preventable 54%).(36)</td>
<td>Fewer whites with preventable AEs 76.1% vs. 72%, p=0.03.(27) Surgical AEs: no effect of race in multivariate analysis.(41)</td>
<td>Main study found no difference.(32) Overall, after age standardisation, 14% of admissions for Maori were associated with an adverse event, compared with 11% for non-Maori/non-Pacific patients (p=0.01 for difference between groups). For preventable in hospital events this disparity persisted after controlling for age, SES and case mix (OR 1.47, p=0.05)(140)</td>
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<td>Socio-economic status</td>
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<td>Slightly higher rate for uninsured patients (?due to age or case mix diff – logistic regression model with age produced no difference). Not insured 17.1% (high preventability 55%, death 0.9%), insured 15.5% (high preventability 42%, death 0.5%)</td>
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<td>No stat sig diff low deep area cf high dep(139)</td>
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<tr>
<td>Co-morbidity</td>
<td>Increase rates of AEs with DRG level</td>
<td>Increased risk of surgical AEs was associated with Charlson score of morbidity ≥4 (OR 1.57, CI 1.03-2.39)(41)</td>
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<td>Medication</td>
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<td>Strobe checklist score (out of 22)</td>
<td>20.5</td>
<td>20.5</td>
<td>21.5</td>
<td>20.5</td>
<td>19</td>
<td>19.5</td>
<td>18.5</td>
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<td>Population</td>
<td>Canada</td>
<td>SW France</td>
<td>Quebec</td>
<td>UK</td>
<td>France</td>
<td>Aberdeen</td>
<td>Spain</td>
<td>Sweden</td>
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<td>Hospitals</td>
<td>20, random selection of 4 hospitals (&lt;250km from research centre, &gt;1500 admissions/year, 24 hour emergency department) from each of 5 provinces - 1 teaching, 1 large community, 2 small community hospitals. No specialty hospitals (paediatric, psychiatric, obstetric, rehabilitation).</td>
<td>7 acute care hospitals, 3 public, 4 private</td>
<td>20, random sample, general acute care hospitals (min 1500 annual admissions and an emergency department, &lt;260km of Montreal)</td>
<td>1</td>
<td>71, public and private. Participation rate 40% (rates=70% in public, 18% in private hospitals)</td>
<td>1</td>
<td>24, 6 small (&lt;200 beds), 13 medium (200-499 beds), 5 large (500+)</td>
<td>28, all large hospitals and a random selection of medium and small hospitals</td>
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<td>No. of records</td>
<td>3745</td>
<td>778</td>
<td>2355</td>
<td>1006</td>
<td>8754</td>
<td>450 then excluded the cases &lt;24 hours as all had no AE, leaving denominator of 354</td>
<td>1967</td>
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<tr>
<td>Method</td>
<td>HMPS (QAHCS 18 triggers)</td>
<td>HMPS retrospective (review of chart 30 days after Two reviewers stage 2 plus</td>
<td>HMPS (18 triggers=QAHC)</td>
<td>HMPS (18 triggers=QAHC)</td>
<td>Prospective (nurse investigators screening - HMPS (15 screening criteria based on Neale(137)) + stage 2 (used)</td>
<td>HMPS (19 criteria - based on IDEA study) + stage 2 (used)</td>
<td>HMPS (18 triggers=QAHCS ) + stage 3 (included mental)</td>
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<td>prospective method) + prospective (collected during hospital stay - day one as cross-sectional, then visits to ward twice during first week and weekly up to 30 days) + cross-sectional (collected in 1 day - interviewed head nurse and if necessary consulted chart, if triggered physician reviewer interviewed the patients doctor and consulted the chart if necessary). Adapted Vincent's questionnaires. 17 triggers (no readmission trigger, documented pain/psychological/social injury finalised in stage 3.</td>
<td>interview senior ward nurse and review records, 16 criteria, if positive doctor investigators interview responsible doc and scrutinise medical record), 3 ward visits over 7 day observation period, HMPS AE definition, Vincent stage 2 forms. All AEs were reviewed by two of the authors to optimise reliability, infections and healthcare product AEs were reviewed by external experts to confirm validity.</td>
<td>consensus stage 3 vs. nurse determination + consensus stage 3 (stage 1a nurses screening using 15 triggers and 1b could identify the AE, summaries of positive charts from 1a (triggered) and 1b (AEs) were reviewed by two clinical researchers who determined which potential AEs to be reviewed by the consensus group in stage 2.)</td>
<td>Vincent forms) + 3rd stage of reviewing uncertain cases by the executive committee</td>
<td>suffering/pain in AE definition). Stage 2 – pairs of physicians, stage 3 – if differing opinions referred to Scientific Council of the National Board of Health and Welfare.</td>
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<td>Sampling</td>
<td>Systematic list sampling (list in order of admission date) - Random sample using CIHI data for all but one province</td>
<td>2 stage cluster stratified process - for each hospital in each stratum selected wards proportional to the number of hospital beds (proportional allocation)</td>
<td>Random sample from all admissions (1/4/00-31/3/01)</td>
<td>Random sample from all admission between Jan-May 2004</td>
<td>Three stage stratified cluster sampling of admissions</td>
<td>150 consecutive patients to each of acute medical admissions, acute surgical admissions, acute obstetric admissions over 1 month</td>
<td>Representative sample. Two state sampling, stratified by hospital size and random selection of hospitals until the appropriate sample size was reached, discharge between 4-10/6/2005</td>
<td>Representative sample of Swedish hospital admissions between Oct 2003-Sept 2004, random selection of medical records (Swedish National Patient Register)</td>
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<tr>
<td>Patient population</td>
<td>&gt;18 years, ≥24 hours stay (or died within 24 hours), exclude MRD related to obstetrics or psychiatry</td>
<td>in-patient medical, surgical and obstetric wards</td>
<td>≥18 years, admitted &gt;24 hours or died within 24 hours. Excl. discharge status unknown, admission due to primary obstetric or psychiatric reasons.</td>
<td>All admissions &gt;24 hours in eight specialties: surgery, urology, orthopaedics, general medicine, medicine for the elderly, oncology, ENT and ophthalmology, excluding psychiatry and obstetrics</td>
<td>in-patients in short-stay, standard and weekday hospital facilities, excl obstetric wards</td>
<td>all admissions to the medical, surgical and obstetric units</td>
<td>in-patient stay&gt;24 hours</td>
<td>Excl admissions to psychiatric clinics, rehabilitation, palliative care and day-only</td>
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<tr>
<td>Adverse event</td>
<td>12 months</td>
<td>12 months</td>
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<td>Trigger 1 - 12 months</td>
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<tr>
<td>review period</td>
<td>before and after</td>
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<tr>
<td>Reviewers</td>
<td>Stage 1 - nurses, stage 2 - physicians. ONE local, one reviewer per chart</td>
<td>Stage 1 - 2 nurse/midwives on the wards - 1 did XS/prospective, the other did retrospective. Stage 2 - 3 doctors in each ward, one for each method</td>
<td>Stage 1 - Trained research nurses, stage 2 - trained physician reviewers (1 per chart)</td>
<td>Stage 1 - Trained nurses, stage 2 - trained hospital doctors (?1 reviewer per chart)</td>
<td>Stage 1 - Nurse investigators, stage 2 - senior hospital practitioners</td>
<td>Stage 1 - Nurses at least 20 years clinical experience, trained in identification of AEs by the National Patient Safety Agency, supervised initially by clinical researcher and senior clinicians. Consensus group - consultant clinicians from various backgrounds, acute sector nursing staff, clinical risk specialist, psychologist, health services researcher.</td>
<td>Stage 1 - Nurses or physicians from each hospital screened charts in stage 1. Stage 2 - external reviewers = research team of 2 trained docs, 1 med, 1 surgical. Uncertain cases were re-analysed by the executive committee. 8 hours training for stage 1 reviewers. Stage 2 - 3 days training, ?1 reviewer per chart</td>
<td>Stage 1 - Trained nurses and stage 2 - experienced physicians, 3 day education programme. Most employed by the Department not the hospital. Stage 2=2 reviewers</td>
</tr>
<tr>
<td>Timing and location</td>
<td>Pre, index and post. AEs that occurred during the index admission. Pre included, not sure about detected post. Prospective and AEs occurring during index, AEs within 12 months before</td>
<td>Pre included, not sure about detected post. Prospective and AEs occurring during index, AEs within 12 months before</td>
<td>Index and post. ?pre included but not stated explicitly. Also Included only AEs that occurred and were detected</td>
<td>Pre, index and post. Included AEs that occurred and detected during index, and pre</td>
<td>Pre, index and post. Included AEs that occurred and detected during index, and pre</td>
<td>Pre (including primary care), index and post.</td>
<td>Pre (including primary care), index and post.</td>
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</table>
and were detected during the index or subsequent hospital admissions over 12/12. AEs related to hospital admissions <12m preceding the index but that were not detected until the index admission. Only hospital admissions occurring in participating hospitals were evaluated.

cross-sectional methods did not include AEs from admission to date of assessment.

index and were detected during index regardless of where the care had been given, AEs detected within 12 months after discharge from index. Only admissions to participating hospitals.

quoted rate after excluding events detected post discharge.

within the 7 day observation period

hospital AEs. pre-hospital (=primary health care, external consultation or previous admission to same hospital). Did not include AEs detected post.

Trigger positive

40.8% 25% 44.5% 31% 32% 33%

Healthcare management causation level

≥4 >4 (and >2) ≥4 ≥4 ≥4 ≥4

% of admissions with ≥1 AE

6.8%, weighted 7.5% (95% CI 5.7-9.3) = of admissions associated with an AE

Retrospective 112 = 14.5% (10.4-18.7) weighted, preventable 4.0%, Prospective 120 = 15.4% (12.2-8.7), preventable

weighted 8.5% (95% CI 7.2-9.8) ≥4 = 8.6% (95% CI 6.9-10.3) [≥2 = 10.9%], also given as 8.7% (7.0-10.4%). If exclude events detected after discharge, incidence =

Incidence density: medicine 6.2% (95% CI 4.9-7.5), surgery 7.0% (5.8-8.3)

8%(=7.9% 95% CI 5.6%-11.2%) Incidence rate of all AEs incl other pre-hospital = 525/5624 = 9.3% (95% CI 8.6-10.1). Exclude non hospital = 473/5624=8.4% (7.7-9.1)

12.3% (10.8%-13.7%)
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<tbody>
<tr>
<td>Events per 100 admissions</td>
<td>7.7</td>
<td>Total list containing AEs generated by 3 methods = 241 AEs in 174 patients</td>
<td>13.5 (≥ 2), 8.6 (≥ 4)</td>
<td>6.6 AEs per 1000 hospital days (95% CI 5.7-7.5)</td>
<td>Incidence density 1.2 AEs per 100 patient days (95% CI 1.1-1.3).</td>
<td>Only the most significant AE was registered and analysed</td>
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<td>Preventable level</td>
<td>≥4</td>
<td>≥4 (sensitivity ≥5)</td>
<td>≥4 (≥ 2)</td>
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<td>% of preventable AEs</td>
<td>41.6%, 15.3% virtually certain, weighted 36.9%. Rate of preventable AEs = 2.8% (95% CI 2.0-3.6)</td>
<td>78/174 (note denominator is all AEs)=45%. Retrospective only = 28%</td>
<td>29%, overall rate 2.7% (95% CI 2.1-3.4)</td>
<td>27% of events, 31% of 87 admissions [≥2 for both causation and prevent: 51%, (55% of 100 admissions)]</td>
<td>35%</td>
<td>43%</td>
<td>43%</td>
<td>70% (8.6% prevalence). Exclude preventable events caused in primary healthcare=8.1% . Incidence of preventable AEs (discovered in index)=8.4%</td>
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<td>Kappa stage 1</td>
<td>0.7</td>
<td>0.70 (0.62-0.78)</td>
<td>0.68 (84% agreement)</td>
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<td>1 (100% agreement)</td>
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<td>0.53 (agreement 79%)</td>
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<tr>
<td>Kappa stage 2</td>
<td>0.47 (injury)</td>
<td>0.83 (agreement 91.7%), low for preventability k=0.51 (agreement 67.8%)</td>
<td>0.64 (agreement 86%), kappa preventability 0.44 (agreement 83%)</td>
<td>agreement 91.7%, kappa 0.83, preventability agreement 67.8%, kappa 0.31</td>
<td>Medical 0.652-0.868, surgical 0.431-0.784</td>
<td>Before discussion - kappa = 0.80 (agreement 91%), preventability kappa=0.76 (agreement 91%)</td>
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<tr>
<td><strong>Sex</strong></td>
<td>no difference in gender</td>
<td>Preventable AEs were more common in females (OR not statistically sig)</td>
<td>No sig diff for AE risk, prev AE risk, severe AE</td>
<td>No stat sig difference</td>
<td>Not stat sig diff</td>
<td>Female 12.8 AEs per 100 (preventable 8.0), male 11.6 AEs per 100 (preventable 9.1)</td>
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<tr>
<td><strong>Age</strong></td>
<td>Those with AEs were sig older mean age 64.9 with AE vs. 62.0 no AE (p=0.016). Risk increases with age.</td>
<td>Preventable AEs were more common in patients 65 years or older (OR not statistically sig). Mean age for preventable AEs 65.9 vs. 61.7 if no preventable AE</td>
<td>No stat sig difference</td>
<td>No stat sig difference</td>
<td>Higher risk if age &gt;65 y 12.4 vs. 5.4%. RR 2.5 (2.0-3.0), p&lt;0.001. Mean age with AE (developed in index) = 64.3y, median 71 vs. no AE mean =52.5 y , median 5</td>
<td>Preventable AEs were more common among patients 65 years and older (OR 1.3 (1.0-1.9)). Rates 0-14 5.0 AE per 100 (preventable 4.4), 15-29 11.7 (preventable 8.1), 30-44 12.5 (8.9), 45-64 12.0 (7.2), 65+ 13.6 (9.9)</td>
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<tr>
<td><strong>Ethnicity</strong></td>
<td>Socio-economic status</td>
<td>Patients with communication problems were more likely to experience multiple preventable AEs (46% vs. 20%, p=0.05). Presence of a</td>
<td>Paper presents increased risk with increasing number of specialties involved in care, this effect for preventable AEs remains significant when</td>
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<td><strong>Co-morbidity</strong></td>
<td>Patients with intrinsic RFs (coma, renal F, diabetes, immunodeficienc y, copd, neutropenia, cirrhosis, drug addiction, obesity,</td>
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<td>physical communication problem was sig assoc with increased risk of preventable AE (OR 3.97, p=0.004). Presence of a psychiatric disorder was sig associated with an increased risk of a preventable AE (OR2.44, p=0.029). Charlson co morbidity not significantly associated with preventable AE risk.</td>
<td>adjusted for co-morbidity (Charlson)</td>
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<td>malnutrition, pressure ulcer, malformations, heart failure, Chad, hypertension = 13.2% AEs vs. 5.2% if no intrinsic RFs, p&lt;0.001, RR 1.6x. Dose response - 1 RF = 10.5%, 2 RF = 15.1%, 3 RF = 22.9%. Trend p&lt;0.001(14). If any co morbidity risk of AE=16.7%, no co morbidity risk = 3.2%, stat sig.(141) The presence of diabetes, neoplasia, chronic pulmonary illness, neutropenia or immunodeficienc y, chronic hepatic alteration, obesity, hypoalbuminaem</td>
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<td>ia, pressure ulcers, cardiac insufficiency, coronary disease or high blood pressure increases the likelihood of experiencing an AE. (141)</td>
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<td>Medication</td>
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<td>Strobe checklist score (out of 22)</td>
<td>20.5</td>
<td>20.5</td>
<td>20.5</td>
<td>21</td>
<td>18</td>
<td>19.5</td>
<td>21.5</td>
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<td>Population</td>
<td>State of Rio de Janeiro</td>
<td>The Netherlands</td>
<td>University hospital Tunisia</td>
<td>Argentina, Colombia, Costa Rica, Mexico, Peru</td>
<td>Egypt, Jordan, Kenya, Morocco, South Africa, Sudan, Tunisia, Yemen.</td>
<td>The Netherlands</td>
<td>Rome hospital</td>
<td>Lisbon</td>
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<tr>
<td>Hospitals</td>
<td>3, teaching hospitals</td>
<td>21, random stratified sample, 4 university, 6 tertiary, 11 general, &gt;=200 beds+ED+ICU</td>
<td>1, general public university hospital</td>
<td>58, 5 each country, purposive sample hospitals, intermediate complexity, needed at least 2000 patients per country</td>
<td>26, convenience sample</td>
<td>(21), 20, (8 hospitals studied in both years), &gt;200 beds and an ICU</td>
<td>1, acute care hospital in-patients (72% in-patients)</td>
<td>3, Lisbon area convenience sample, excluded specialty hospitals (paediatrics/oncology/obstetrics)</td>
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<tr>
<td>No. of records</td>
<td>1103 (non-obstetric=80.5%)</td>
<td>7926</td>
<td>620</td>
<td>11332</td>
<td>15548</td>
<td>7887 (2004) + 3996 (2008) = 11949. Note denominator in 2004 was 7926 but some charts were not able to be linked and had missing diagnostic info therefore</td>
<td>1501</td>
<td>1669</td>
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<tr>
<td><strong>Method</strong></td>
<td>HMPS (18 triggers=QAH CS)</td>
<td>HMPS (18 triggers=QAH CS)</td>
<td>Point prevalence, HMPS + stage 1= IDEA 19 triggers + stage 2 = Eneas forms adapted from Vincent forms. Patients screened for AEs only in the 24h immediately prior to the review, regardless of when the patient was admitted</td>
<td>HMPS, 18 triggers=QAH CS</td>
<td>HMPS, 716 or 18 triggers=QAH CS</td>
<td>HMPS (Vincent), 16 triggers</td>
<td>HMPS (18 triggers=QAH CS?)</td>
<td>Prospective recruitment and patient survey, HMPS retrospective chart review (QAHCS 16/18 triggers, not injury related to abortion/labour/delivery or documentation indicating litigation, Zegers design) at 4 months post discharge</td>
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<tr>
<td><strong>Sampling</strong></td>
<td>Random sample of 27350 admissions</td>
<td>Random sample of 200 discharges and 200 deceased. Only included records with both the nursing and medical records present</td>
<td>stratified random sampling, sample size was proportional to the number of admissions in each of the 18 clinical departments</td>
<td>all patients admitted during 1 week in 2007</td>
<td>Random selection of &gt;600 patient records from the list of all admissions at each hospital</td>
<td>Random sample of 200 admissions in 2008 *400 in 2004), 50% discharged after a stay of at least 24 hours, 50% died in hospital regardless of length of stay (cf actual =</td>
<td>Random sample, representative, discharged 1/1/2008-31/12/2008</td>
<td>At each hospital a random sample was selected</td>
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<td><strong>Patient population</strong></td>
<td>≥18 years old, excl stay &lt;24 hours and psychiatric diagnoses</td>
<td>&gt;24 hour, excluding admissions to psychiatry and obstetrics and children &lt;1 year</td>
<td>In-patients from all 18 clinical departments</td>
<td>all patients</td>
<td>Medical, surgical, paeds, obstetric in-patients in acute care public or private hospitals. No same day (but 2215 cases were inadvertently included).</td>
<td>Excluded patients admitted to psych dpt, obstetrics and children&lt;1 year</td>
<td>In-patients all ages, &gt;24 hours hospital stay. No day cases.</td>
<td>&gt;18 years, stay ≥24 hours, exclude primary diagnosis related to psychiatry</td>
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<td><strong>Adverse event review period</strong></td>
<td>12 months before and after</td>
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<tr>
<td><strong>Reviewers</strong></td>
<td>Physicians and nurses&gt;20year experience, stage 2=1 reviewer?</td>
<td>Trained nurses and doctors. Reviewed nursing, medical and if available outpatient record.</td>
<td>Trained medical student - stage 1, two expert physician independently reviewed</td>
<td>Stage 1 - nurse or clinical physician, stage 2 = physician (at least 5 years</td>
<td>Stage 1 - nurses or junior docs. Stage 2 - one physician per chart. Experienced</td>
<td>Stage 1 - Trained external nurses and stage 2 - trained external</td>
<td>Stage 1 - two physicians, stage 2 - 2 reviewers independently assessed each record, if</td>
<td>Trained and experienced nurses and specialists (nurse decided whether stage 2 was done by</td>
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<tr>
<td>Timing and location</td>
<td>Stage 1 - nurses, stage 2 - two doctors independently reviewed each triggered record ***also determined life expectancy in deceased cases. Stage 3 - consensus if disagreement in stage 2, if no consensus then a third doc reviewer gave the final judgement.</td>
<td>triggered charts (stage 2 two reviewers, if disagreed then discussion to judge presence of AE)</td>
<td>experience), could be from same hospital, ?1 reviewer per chart</td>
<td>nurses and senior doctors (int med, surgical or anaesthetic bkgrds). Stage 2 = 1 reviewer</td>
<td>physicians - surgery., internal med and neurology (+consultation with other specialties if reqd). Mostly the same reviewers for both studies. One reviewer per chart in 2008, two in 2004.</td>
<td>disagreement on presence of AE had discussion if still disagreed then went to a final reviewer to make the decision. 2.5 days theoretical-practical training course. ***Unclear if the stage 1 and 2 reviewers were the same??</td>
<td>stage 2 - physicians (cardiologist, neurologist, surgeons, int med) min 5y experience in clinical codes and audits</td>
<td>int med, surgeon or neurologist, did not review charts in own hospitals</td>
</tr>
<tr>
<td>Trigger positive</td>
<td>41% (exclude obstetrics)</td>
<td>54%</td>
<td>11.7%</td>
<td>33.9%</td>
<td>8.1%</td>
<td>22%</td>
<td>48% ethnic, 51% Dutch</td>
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<p>| Not stated. Results indicate out of hospital locations - home and other place. | Pre, index and post | Point prevalence. Patients screened for AEs only in the 24h immediately prior to the review, regardless of when the patient was admitted | AE could occur before and contributed to the index or during the index | AE pre and post, related to index hospital | During index, plus detected &lt;12months. No pre hospitals AEs |
|-------------------|-----------------------------------------------|-------------------------------------|--------------------------------------|------------------------------------------|------------------------|----------------------------------|---------------------------------|----------------------------------|-------------------------------|
| 44.5%             |                                               |                                     |                                      |                                          |                        | overall 49.7%                    |                                 |                                  |                               |
| Healthcare management causation level | ≥4                                             | ≥4                                  | ≥4                                   | ≥2                                       | ≥4                     |                                  |                                 |                                  |                               |
| % of admissions with ≥1 AE | 84 (7.6%). Exclude obstetric – 8.6% | 5.7% (95% CI 5.1-6.4%). Incid of AEs in deceased=10. 7% | 10% (95% CI 7.6-12.3) | 10.5% (9.91-11.04). Range per country 7.7-13.1% | Causation ≥2: 8.2% (range for countries 2.5-18.4%), if exclude day admissions then AE rate 8.8%, if exclude obstetric hospitals 11.6%, if increase causation to ≥4=6.1% | weighted 4.1% (95% CI 3.3-5.1) + 467/3996 = weighted 6.2% (5.0-7.6) | 3.3%                           | 11.1% (95% CI 9.6-12.6) | Dutch 11.4% (95% CI 9.1-13.7), ethnic = 9.9% (95% CI 7.5-12.3), overall = 10.8% |
| Events per 100 admissions or patient days | 9.3 per 100 patients (=103/1103). Incidence density=0.8 per 100 patient days (0.6-0.9) | 4 events/1000 hospitalisation days | AE ratio=11.85% | Only 1 AE per patient | Only 1 AE per patient | rate per 1000 patient-days: 2004=6.0, 2006=10.5. | Only one AE per admission was analysed (the most serious one) |                               |                               |
| Preventable level | ≥4                                             | ≥4                                  | ≥4                                   | ≥4                                       | ≥4                     |                                  |                                 |                                  |                               |</p>
<table>
<thead>
<tr>
<th>% of preventable AEs</th>
<th>66.7%, non-obstetric=65.8%</th>
<th>45%, weighted, 2.3% overall, deceased=5.2%</th>
<th>Incid of</th>
<th>60%</th>
<th>59%, overall prevalence=5. 49% (95% CI 5.07-5.91)</th>
<th>83% (55-93% country range)</th>
<th>weighted 1.8% (1.3-2.4) + 198 (2008) = weighted 1.6% (1.2-2.3).</th>
<th>53.2%</th>
<th>Dutch 2.6% (1.5-3.8), ethnic 1.0% (0.21-1.87)</th>
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<tr>
<td>preventable AEs contributing to death in deceased</td>
<td>4.1%</td>
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<tr>
<td>Overall</td>
<td>37.5%</td>
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<tr>
<td>Kappa stage 1</td>
<td>0.62</td>
<td>0.67</td>
<td>Pilot study - two countries</td>
<td>0.85, 0.55</td>
<td>0.33-0.88</td>
<td>0.62 in 2004, 0.65 in 2008</td>
<td></td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td>Kappa stage 2</td>
<td>Not tested – one physician</td>
<td>0.25</td>
<td>0.82</td>
<td>Pilot study - 5 countries AE (prev AE)= x (0.62), 0.87 (0.74), 0.32 (x), 0.38 (0.47), 0.30 (0.27)</td>
<td>not completed</td>
<td>0.25 in 2004, 0.47, prev AE 0.4 and 0.49</td>
<td></td>
<td></td>
<td>0.78 (preventability 0.58)</td>
</tr>
<tr>
<td>Sex</td>
<td>No stat sig in multilevel logistic regression(40)</td>
<td>No stat sig diff between male and female</td>
<td>No difference</td>
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<td></td>
<td></td>
<td>No difference</td>
<td>No stat sig diff p=0.418</td>
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<tr>
<td>Age</td>
<td>proportion of AEs, preventable AEs and degree of disability increased with age. 1-18 1.7% AEs, 20% prev, 19-40 5% AEs, 40% prev, 7%</td>
<td>No diff between age group bands for risk of AE</td>
<td>Not retained as an independent variable or as a confounding factor. Exception in preventable AEs - higher in children aged under 1y and also as the patient ages in Graph showing increasing AE rate with increase in age</td>
<td>Increased risk of AEs and prev AEs with age</td>
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<td></td>
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<td>No stat sig</td>
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<td>Most of the AEs occurred in patients aged 65 or over. 59.2% of patients who experienced an AE were 65+. Figure shows increasing risk with increasing age.</td>
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<td>perm, 2% death, 41-65 5.5% AEs, 37.5% prev, 2.4% perm, 4.3% death, 66-79 6.1% AEs, 40% prev, 4.3% perm, 12.3% death, 80+ 8.2% AEs, 46.2% prev, 9.8% perm, 15.2% death. (31) multilevel logistic regression: age (years) = OR 1.02 (1.01-1.02). Increasing age and co-morbidity was associated with increased risk of preventable AEs (40). AEs and Prev AEs occur sig more often in older patients (6.9%)</td>
<td>general</td>
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---|---|---|---|---|---|---|---|---|---|
and 2.9%) cf younger patients (4.8% and 1.8%)(144) | | | | | | | | No stat sig diff for AE rate or preventable AE rate or for impact of AEs. No diff in OR (three multivariate regression models) | |
Ethnicity | | | | | | | | | |
Socio-economic status | | | | | | | No diff for intrinsic risk factors | Looked at residence (local/other), citizenship, marital status - none stat sig |
Co-morbidity | increasing age and co-morbidity was associated with increased risk of preventable AEs. multilevel logistic regression: Charlson OR=1.23 (1.11-1.4 ), No diff for intrinsic risk factors | Increased risk with (any) co-morbidity OR 1.42 (95% CI 1.22-1.64) | | | Both 2004 and 2008: Increased risk (higher ORs) for digestive system, injury and poisoning, genitourinary and neoplasms (ref circulatory) (=AEs and especially prev | No association of AEs with co-morbidity assessed by Charlson Index |

256
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<tr>
<td>Medication</td>
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<td>21.5</td>
<td>17</td>
<td>21</td>
<td>18.5</td>
<td>21</td>
<td>18.5</td>
<td>21</td>
<td>18.5</td>
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<tr>
<td>Strobe checklist score (out of 22)</td>
<td>18.5</td>
<td>21.5</td>
<td>17</td>
<td>21</td>
<td>18.5</td>
<td>21</td>
<td>18.5</td>
<td>21</td>
<td>18.5</td>
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<tr>
<td>prev AEs OR=1.38 (1.19-1.60)(40)</td>
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</table>
Appendix 5: Hospital invitation letter and op-in form

1 May 2013
Title Firstname Lastname
Address1
Address2
City, Postcode

Re: National Adverse Event Study: Irish Acute Hospitals

Dear Title Lastname,

Our research group is undertaking an important national study of the prevalence and nature of adverse events in Irish acute hospitals. The study is funded by the Health Research Board (HRB) under the HRB/HSE framework for advancing the research agenda in quality and patient safety and has been approved by the Research Ethics Committees of the Royal College of Physicians of Ireland and the Royal College of Surgeons in Ireland. It is also supported by the Presidents of each College.

The study will provide important baseline data on adverse events for Ireland and will identify areas for improvement and assist in the evaluation of patient safety and improvement initiatives. As Adverse Event (AE) rates are usually discovered during a review of patient case notes, we will use this internationally-accepted, 2-stage process to assess AEs in Irish acute hospitals:

1. Nurses screen a random sample of notes using criteria that could indicate an AE
2. Physicians then review these notes to establish whether an AE has taken place and identify any associated consequences

The study will involve the review of approximately 1700 patient case notes across eight hospital sites. We are writing to all acute hospitals (excluding maternity and paediatric) inviting participation in this important study. All notes and hospital details will be irrevocably anonymised for analysis making it impossible to identify individual patients, clinicians or institutions. AE prevalence results will also be compared with adverse event rates as recorded through hospital CStar reporting systems. Your hospital will be provided with the final report, which will consist only of aggregated national results.

The benefits for your hospital will be gained through studying the resulting national trends in AE occurrences. It will be possible to identify the conditions that heighten the chances of unintended patient harm and will facilitate the design of interventions for improving patient safety leading to a reduction in AE rates and associated costs.

We are asking for your permission to review clinical notes within your hospital. A team of two experienced research nurses and two medical clinicians will be specially trained for this study and they will undertake a retrospective chart review of approximately 200 case notes in your hospital from a period in 2006.

We will select a random sample of 8 hospitals from a group of Irish Hospitals willing to participate in this study. If you would be willing to be selected randomly to participate please tick the appropriate box on the enclosed form and return it in the stamped, addressed envelope provided.

Registered Charity in Ireland Ref. OY1897
Yours sincerely,

[Signature]

Prof David Williams, Principal Investigator
Associate Professor of Geriatric Medicine
RCSI/Beaumont Hospital
Please tick the appropriate box below and return your answer in the stamped addressed envelope provided. Thank you.

**Yes**, our hospital would be willing to be randomised to participate in the Irish National Adverse Events Study (INAES)  

If we are randomised to participate in the study, we would like to meet the research team to learn more about the INAES study

**No**, our hospital would not like to be randomised to participate in the INAES study

Hospital name:
Appendix 6: Hospital consent form

Irish National Adverse Event study (INAES)

PI Professor David Williams

Hospital Consent Form

I consent to participation in the Irish National Adverse Event Study (INAES) on behalf of ......................... Hospital, Ireland.

Signed

Date

Print Name

Role
Appendix 7: Ethical approval letters

Royal College of Surgeons in Ireland
The Research Ethics Committee
121 St. Stephens Green, Dublin 2, Ireland.
Tel: +353 1 4022273  Fax: +353 1 4022205  Email: recadmin@rcsi.ie

Dr. David Smith, Acting Chair
Dr. Niamh Clarke, Convenor

15th April 2013

Prof David Williams
Department of Geriatric and Stroke Medicine
Beaumont Hospital,
Dublin 9

<table>
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<th>Ethics Reference No:</th>
<th>REC815</th>
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<tr>
<td>Project Title:</td>
<td>Irish National Adverse Events Study.</td>
</tr>
<tr>
<td>Researchers Name:</td>
<td>Prof David Williams</td>
</tr>
<tr>
<td>Other Individuals Involved:</td>
<td>Prof. Ann Hickey Department of Psychology, RCSI. Dr. David Vaughan National Clinical Programme, HSE. Dr. Sarah Condell BNurs, MA, PhD, Nursing &amp; Midwifery Research and Development, HSE. Gillian Walsh BSc Research Department, RCPI. Dr. Paul O' Connor Primary Care Department, NUI. Prof. Ronan Conroy Associate Professor of Biostatistics, Dept of Epidemiology and Public Health Medicine, RCPI.</td>
</tr>
</tbody>
</table>

Dear David,

Thank you for your Research Ethics Committee (REC) application. We are pleased to advise that ethical approval has been granted by the committee for this study.

This letter provides approval for data collection for the time requested in your application and for an additional 6 months. This is to allow for any unexpected delays in proceeding with data collection. Therefore this research ethics approval will expire on 1st January 2016.

Where data collection is necessary beyond this point, approval for an extension must be sought from the Research Ethics Committee.

This ethical approval is given on the understanding that:
- All personnel listed in the approved application have read, understand and are thoroughly familiar with all aspects of the study.
- Any significant change which occurs in connection with this study and/or which may alter its ethical consideration must be reported immediately to the REC, and an ethical amendment submitted where appropriate.
- Please submit a final report to the REC upon completion of your project.

We wish you all the best with your research.

Yours sincerely,

[Signature]

PP Dr. Niamh Clarke (Convenor)
Dr David Smith (Acting Chair)
10 September 2013

Prof David Williams
Department of Geriatric and Stroke Medicine
RCSI/Beaumont Hospital
Beaumont Road
Dublin 9

Re: Irish National Adverse Events Study (INAES)
ID: RCPI RECSAF 04

Dear Prof Williams,

Many thanks for sending your revised RECSAF with amendments for INAES.

The Research Ethics Committee’s opinion is favourable.

The committee raised the following points.

1. While you have not provided for a specific feedback mechanism in regard to individual cases where adverse events have occurred the points made in regard to overall feedback, use of similar protocols elsewhere and the lagtime in review are reasonable.

2. As the other local involvement and processes that were suggested are also now part of the audit protocol it is my opinion as chair of the REC that this important audit should proceed as outlined.

The committee would like to wish you every success in undertaking this project.

Yours sincerely,

[Signature]

Dr Davida De La Harpe
Appendix 8: Hospital information to staff about INAES

Re: National Adverse Event Study: Irish Acute Hospitals Announcement

The National Adverse Study research group is undertaking an important national study of the prevalence and nature of adverse events in Irish acute hospitals. The study is funded by the Health Research Board (HRB) under the HRB/HSE framework for advancing the research agenda in quality and patient and has been approved by the Research Ethics Committees of RCPI and RCSI. It is also supported by the Presidents of each College. Our hospital <hospital name> has been selected as one of the eight participating hospital sites.

The study will provide important baseline data on adverse events for Ireland and will identify areas for improvement and assist in the evaluation of patient safety and improvement initiatives. As Adverse Event (AE) rates are usually discovered during a review of patient case notes, we will use this internationally-accepted, 2-stage process to assess AEs in Irish acute hospitals:

1. Nurses screen a random sample of notes using criteria that could indicate an AE
2. Physicians will then review these notes to establish whether an AE has taken place and identify any associated consequences

The study will involve the review of approximately 1700 patient case notes across eight hospital sites. A team of research nurses and two medical clinicians will be specially trained for this study and they will undertake a retrospective chart review of approximately 200 case notes in our hospital from a period in 2009. All notes and hospital details will be irrevocably anonymised for analysis making it impossible to identify individual patients, clinicians or institutions. National AE prevalence results will also be compared with adverse event rates as recorded through hospital STARSweb reporting systems. Our hospital will be provided with the final report, which will consist of aggregated national results.

The benefits for our hospital will be gained through studying the resulting national trends in AE occurrences. It will be possible to identify the conditions that heighten the chances of unintended patient harm and will facilitate the design of interventions for improving patient safety leading to a reduction in AE rates and associated costs.

This 2 year study will start in October 2013 and results will be published in late 2015.
Appendix 9: HIPE summary sheet

### Hospital In-Patient Enquiry (HIPE) Summary Sheet

*For use with WH-HE data entry software on ALL DISCHARGES FROM 01.09.08*

#### Patient Details

- **Medical Record Number**: 
- **Type (priority) of admission**: 
- **Source of admission**: 
- **Date of transfer to PDU/PDHU**: 
- **Discharge Date**: 
- **Date of birth**: 
- **Sex**: 
- **Mode**: 
- **WEI**: 
- **Weight (kg)**: 
- **Temporary Leave Days**: 

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<tr>
<th>Field</th>
<th>Information</th>
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<tbody>
<tr>
<td>Name</td>
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<tr>
<td>Medical Card</td>
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<tr>
<td>Day Case</td>
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<tr>
<td>Day Ward</td>
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<td>Marital Status</td>
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<td>GMS Number</td>
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<td>Discharge Status</td>
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<td>Discharge Ward</td>
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<tr>
<td>Days in Intensive Care Environment</td>
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<tr>
<td>Days in Private/Semi Private Bed</td>
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<tr>
<td>Up to 10 Intensive Care consultants may be recorded</td>
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#### Principal Diagnoses

**ICD-10-AM Code**

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<thead>
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<th>Principal Diagnosis (PDx)</th>
<th>Consultant</th>
<th>Specialty</th>
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#### Procedures

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<th>Principal Procedure</th>
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<th>Consultant Assistant</th>
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#### Dates

- **Date of First Procedure**: / / 
- **Date of Principal Procedure**: / / 

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Source: HIPE Unit, Health Research & Information Division, ESRI, Whitaker Square, St John Rogerson’s Quay Dublin 2. Tel: 01-8632000

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Appendix 10: Guidance for the HIPE office and medical records department

Irish National Adverse Event study (INAES) Chart selection

Guidance notes for the HIPE Office and Medical Records Department

Thank you for agreeing to participate in the Irish National Adverse Events Study (INAES).

The study aims to quantify the prevalence and nature of adverse events in major acute hospitals across Ireland. To do this approximately 200 of your patient charts will be reviewed by trained nurse and physician reviewers using an international methodology. The charts will be selected randomly from a list of adult inpatients who were admitted during 2009, elective and emergency, to any medical or surgical specialty but excluding patients with psychiatric or obstetric principal diagnoses.

Please note that patient data and participating hospitals will be anonymised in the study.

HIPE office

Hospital In-Patient Enquiry (HIPE) portal search strategy

1. Basic search
   • Admission date between 01/01/2009 and 31/12/2009, discharge date 01/01/2009-31/12/2012
   • Inpatient
   • Patients age in years between 18 and 110
   • Admission source post 2002 is not between 3 and 4 (i.e. exclude transfers from other acute hospitals)
   • Principal diagnosis is not between F00 and F99 (i.e. exclude psychiatric)
   • Principal diagnosis is not between O29 and O927 (i.e. exclude obstetric)

2. Surgery charts
   • Basic search plus
   • The All Procedures (ICD-10-AM) is between 9251400 and 9251499 (i.e. general anaesthetic)
   • The All Procedures (ICD-10-AM) is between 9250800 and 9250899 (i.e. neuroaxial block)
   • The All Procedures (ICD-10-AM) is between 9250900 and 9250999 (i.e. regional block, nerve of head or neck)
   • The All Procedures (ICD-10-AM) is between 9251000 and 9251099 (i.e. regional block, nerve of trunk)
   • The All Procedures (ICD-10-AM) is between 9251100 and 9251199 (i.e. regional block upper limb)
   • The All Procedures (ICD-10-AM) is between 9251200 and 9251299 (i.e. regional block lower limb)
   • Use the HIPE portal Reporter to randomly select 150 charts. These are the surgery charts for review.

3. Non surgery charts
   • Basic search plus edit the procedures to ‘is not’
The All Procedures (ICD-10-AM) is not between 9251400 and 9251499 (i.e. no general anaesthetic)
- The All Procedures (ICD-10-AM) is not between 9250800 and 9250899 (i.e. no neuroaxial block)
- The All Procedures (ICD-10-AM) is not between 9250900 and 9250999 (i.e. no regional block, nerve of head or neck)
- The All Procedures (ICD-10-AM) is not between 9251000 and 9251099 (i.e. no regional block, nerve of trunk)
- The All Procedures (ICD-10-AM) is not between 9251100 and 9251199 (i.e. no regional block upper limb)
- The All Procedures (ICD-10-AM) is not between 9251200 and 9251299 (i.e. no regional block lower limb)
- Use the HIPE portal Reporter to randomly select 150 charts. These are the non surgery charts for review.

4. Export the following fields into excel (in order) for the surgery cases and for the non surgery cases [show diagnosis/procedure description in patient reports]:
   - Medical Record Number
   - Name
   - Date of birth
   - Patient Age in years
   - Sex of patient
   - Admission Type
   - Admission Date
   - Discharge Date
   - Length of stay
   - Number of ITU Days
   - Specialty
   - Medical card
   - Australian Refined Diagnosis-Related Group (AR-DRG)
   - Principal Diagnosis and ICD-10 code
   - Additional Diagnosis 1 (plus all additional diagnoses) and ICD-10-AM code (plus all additional diagnoses ICD-10-AM codes)
   - Principal Procedure and procedure code
   - Additional Procedure 1 and procedure code (plus all additional procedures and codes)

   Thus two excel spreadsheets will be produced – one with the surgery charts and with the non surgery charts.

5. A unique study ID number (e.g. D_001, D_002, etc) is assigned to each MRN. The study ID will replace the identifiable patient details (MRN, name, date of birth) in the excel spreadsheets prior to being uploaded in the INAES database. The full excel lists of MRN, name, date of birth, and matching study ID (i.e. the master MRN/study ID look up lists) will be kept in the hospital for use by the INAES nurse and physician reviewers.

6. The HIPE office will provide the two lists to the Medical Records Department for chart retrieval.

Medical records

We would request the Medical Records Department obtain the following for the patient charts on the lists:
- Documentation relating to the index admission
- Admission notes
- Progress notes
- Consultant’s notes
- Nurses’ notes
- Procedure notes (theatre)
- Consents
- Medication prescribed/administration records
- Laboratory records (Chemistry, Haematology, Microbiology etc)
- Diagnostic Imaging
- Blood Bank
- ICU/ITU/CCU/HDU/ED notes

- Plus all previous admissions of the same patient 12 months prior to the index admission (defined below) and 12 months after the index admission including all of the above listed documentation for these previous and subsequent admissions.

It is recommended that the charts are retrieved in batches from each excel spreadsheet (surgery and non surgery) starting at the top of the two lists. For example the first 50-100 from each list should be retrieved and reviewed by the INAES nurse initially. Prior to the nurse finishing the first batch, the Medical Records Department should start the retrieval of the second batch from each list.

Around 200 charts are required to be reviewed at each hospital site, therefore once 100 surgery and 100 non surgery charts have been reviewed no further charts will be needed. An oversample of 300 will be randomly selected to account for missing or incomplete charts and those who do not satisfy the inclusion criteria (e.g. included patients must have had a hospital stay of at least 24 hours or have died within 24 hours).

**Electronic Records**

It is understood that some of the information required above may be in electronic format. In this case the INAES reviewers will need access to, and training on the appropriate system, to conduct the review. Ideally reviewers should have access to the patient's paper and electronic records simultaneously while conducting the review.

**Tracking of charts during review**

The MRN/study ID look up lists will be stored securely in the hospital. They will serve as a reference for the Medical Records Department staff and INAES reviewers for the duration of the nurse and physician chart reviews only and will be destroyed on completion of all the chart reviews at the hospital. The lists will allow the INAES nurse and physician reviewers to ensure that they are reviewing the correct patient chart and to ensure that any supplementary hospital information e.g. from electronic systems, relates to that patient.

The INAES reviewers will use the MRN/study ID look up lists to enter the review information in the INAES database. For example, the reviewer selects a chart with MRN=5656589 and refers to the MRN/study ID lists for the corresponding study ID. The reviewer then enters the study ID into the INAES database and proceeds with the review under the study ID.

**Definition of terms**

**Index admission:** The index admission is the episode of care (admission) which is the focus of the chart audit for each case under review.
Appendix 11: Example HIPE search screen shot
Appendix 12: INAES Operations Manual description of nurse triggers

Trigger 1 Unplanned admission (including readmission) as a result of any healthcare management within the 12 months prior to the index admission

An adverse event may have been the result of care delivered in a previous hospitalisation but not detected until the patient is admitted at the time of the index hospitalisation. The nurse reviewer looked for evidence in the index admission that indicated an unplanned hospitalisation occurring within the 12-month period preceding admission. The hospitalisation may have been at the index or any other hospital but unless documents were forwarded as part of an inter-hospital transfer it was not possible to access the charts of previous admissions occurring at another institution. The index admission must indicate there a link to previous care. Situations in which this trigger may have applied include:

- Admission or re-admission for complications
- Admission or re-admission for problems arising due to incomplete management of problems identified on previous hospitalisation
- Admission or re-admission as the result of healthcare management in the absence of exceptions, including management at other healthcare facilities, primary care, medical centres, allied and alternative health professional care.
- Recurrence of a presumably cured disease
- Complications of previous procedures
- Inadequate follow up of a previously treated problem
- Premature discharge on previous admission

The following situations were specifically excluded:

- Elective admissions for secondary procedures needed to complete treatment.
- Previous or subsequent admission for a normal delivery.
- Prior hospitalisations unrelated to the index admission
Examples given in the Operations Manual for trigger #1 included:

1. Patient admitted June '97 for mastectomy. Pathology reported a complete excision. Patient was readmitted seven months later with metastatic cancer.

2. Patient admitted in a diabetic coma. Patient was previously discharged 14 days following an admission for newly diagnosed diabetes - no evidence of recommended follow-up with the patient's general practitioner (GP), no letter to the GP, or instructions for continued outpatient care appeared in the medical record.

*Trigger #2: Unplanned admission to any hospital within a period of 12 months after discharge from index admission*

An adverse event may have been the result of care delivered in the index admission but the event may not be detected until a subsequent admission. Therefore the nurse reviewer looked for evidence of an unplanned hospitalisation occurring within the 12 month period following discharge from the index hospital stay. All admissions occurring at the index hospital within 12 months following the day of the index admission were reviewed. Unless documentation was present in referral notes or discharge summaries admissions to other institutions occurring within this time period were not able to be captured.

The following scenarios were included in this trigger:

- Readmission for complications following the index hospitalisation
- Admission or re-admission for problems arising due to incomplete management of problems identified during the index admission
- Recurrence of a presumably cured disease
- Complication of previous procedures
- Inadequate follow up of a previously treated problem
- Premature discharge on the first admission
Subsequent hospitalisations unrelated to the index and transfers or admissions to other facilities for rehabilitation or ongoing care were excluded.

Examples of trigger #2 given in the Operations Manual included:

1. Patient discharged following a total hip replacement. Patient required blood transfusion during the operation. Patient readmitted three months later with hepatitis.

2. Patient discharged following an acute myocardial infarction (MI). No discharge medications were prescribed. Patient was readmitted seven days later with a second MI.

Trigger #3: Hospital incurred patient injury (including any harm, injury or trauma occurring during the index hospitalisation)

The nurse reviewer examined the patient chart for evidence of any harm, injury, or trauma incurred during the index hospitalisation. The trigger must have been the result of treatment or care delivered during the index admission and not progression of disease. This included burns, falls, infection (symptoms >48 hours post admission), medication errors, procedural errors, decubitus ulcers (threatened or new). Accidents with no related injury were not included (e.g. a patient assisted to bed by two nurses falls to their knees but no injury occurs).

Examples given in the Operations Manual of trigger #3 included:

1. 17 mls of methadone administered instead of 17 mgs. Patient required gastric lavage and 1:1 nursing observation for 24 hours.

2. Patient receiving naso-gastric feeds developed aspiration pneumonia. Patient was over sedated.

3. Patient developed pulmonary oedema secondary to rapid infusion of intravenous fluids.
Trigger #4: Adverse drug reaction

The nurse reviewer looked for evidence in the medical record of an adverse drug (medication) reaction. The adverse drug reaction may have occurred (1) in response to a drug given prior to the index admission, (2) in response to a drug given during the index admission or (3) the drug may have been given during the index hospitalisation but the adverse reaction may not have occurred until after discharge. Reviewers were instructed to select yes if there was evidence of response to or treatment for an adverse drug reaction, unexpected transfer to intensive care, or unexpected admission to hospital.

This trigger included:

- Allergic reactions
- Anaphylaxis
- Adverse reactions.
- Hives
- Severe nausea and vomiting following drug administration
- Toxic drug levels leading to morbidity
- Iatrogenic acute tubular necrosis following antibiotic treatment
- Gastrointestinal bleeding following aspirin administration.
- Severe hypoglycaemic reaction in a patient on insulin or oral hypoglycaemics

Examples given in the Operations Manual for trigger #4 included:

1. Following administration of penicillin, a patient developed acute respiratory distress requiring administration of adrenaline and steroids.

2. During day surgery for breast biopsy, a patient developed severe nausea and vomiting post-op, given prochloperazine, developed severe hypotension and syncope, admitted to hospital for 5 days.

3. Patient received sedation– bedsides were not raised – and tried to get out of bed on own to go to the bathroom, fell from bed and lacerated forehead on
bedside table. Note this scenario would also satisfy trigger #3 of hospital incurred patient injury. In this case the nurse reviewer would have triggered both #3 and #4.

*Trigger #5: Unplanned transfer from general care to intensive care*

The nurse reviewer examined the chart for evidence of an unexpected or unplanned transfer from an inpatient medical or surgical unit to an intensive care (ICU) unit, or critical care unit during the index hospitalisation. The admission to intensive or critical care may have occurred unexpectedly when a patient's clinical condition deteriorated or post-operatively perhaps secondary to an adverse event. Patients that were expected to be moved to higher levels of care as a part of their routine care delivery, i.e. to ICU following cardiovascular surgery, did not qualify for this trigger. Similarly if the ICU was being used as a recovery room (e.g. in small hospitals) or an observation or holding area until a ward bed became available, this event would not be triggered.

Examples given in the Operations Manual for trigger #5 included:

1. Multi trauma patient with no loss of consciousness admitted to the emergency department (ED). Patient became unconscious 3 hours post admission, CT showed subdural haematoma. Patient was operated on with burr holes then transferred to ICU. There was no record of neurological observations being performed in ED.

2. Asthmatic patient transferred to ICU from the ward with respiratory failure. No peak flows recorded since admission and a four hour delay notifying medical staff was noted.
Trigger #6: Unplanned transfer to another acute care hospital (excluding transfers for tests, procedures, or specialised care not available at referring hospital)

The nurse reviewer looked for evidence in the patient chart of an unexpected or unplanned transfer to another acute care hospital. The hospital transfer may have been either (1) into the index hospital (however most of these will have been excluded at the time of the HIPE search) or (2) out of the index hospital. Transfers for tests, procedures or special care were included only if they were required due to an unexpected deterioration in the patient’s condition.

An example given in the Operations Manual for trigger #6 was:

1. Anaphylactic reaction during induction of anaesthetic required transfer to a tertiary referral centre for intensive care management.

Trigger #7: Unplanned surgery or return to the Operating Room

The nurse reviewers looked for any evidence in the medical record of an unplanned surgery or an unexpected return to the operating room during the index hospitalisation or following discharge. This included repeat surgery on the same day, after-hours surgery, and a medical patient undergoing surgery for a procedure not usually included in their continuum of care. Planned second procedures or second stage of a procedure were not included.

An example given in the Operations Manual for trigger #6 was:

1. Three days post bowel surgery patient developed severe abdominal pain, 8 hours later the patient had surgery (?delay) for repair of anastomotic leak, gross faecal soiling and peritonitis.
**Trigger #8: Unplanned removal, injury or repair of organ or structure during surgery, invasive procedure or vaginal delivery**

Nurse reviewers looked for evidence in the medical record that the patient had required the removal of or repair to a laceration, perforation, tear or puncture of an organ during the index hospitalisation. This may have manifested as: (a) immediate injury, e.g. ruptured spleen intra-operatively requiring splenectomy; or (b) a late complication. E.g. post biopsy bleeding due to damage to another organ requiring surgery for repair. Reviewers were instructed to read all operative notes carefully to look for intra-operative injuries. Cases of injury with no sequelae were not triggered, e.g., the spleen is nicked and repaired during a colectomy, there is no requirement for splenectomy or blood transfusion or a return to the operating room, and no readmissions after discharge. Reviewers were advised that if they were unsure whether an injury had caused sequelae then the trigger should be chosen.

Examples given in the Operations Manual for trigger #8 included:

1. Uncomplicated kidney biopsy but pathology report indicates splenic tissue.

**Trigger #9 Other patient complications e.g. AMI, CVA, PE etc. (includes any unexpected complication occurring during the index admission that is NOT a natural progression of the patient’s disease or an expected outcome of treatment)**

The nurse reviewers looked for evidence in the patient chart that the patient had experienced any event that had no direct causal relationship to the patient’s treatment, surgery or procedures performed and that was not an
expected outcome or natural progression of the disease. The fact that a complication occurred during hospital admission in the absence of a causal relationship meant the requirements for this trigger were met.

Examples given in the Operations Manual for trigger #9 included:

1. Patient developed a deep vein thrombosis ten days post-operatively.
2. Unstable angina four hours post-operatively, transferred to coronary care

_Trigger #10: Development of neurological deficit not present on admission but present at the time of discharge from the index hospital stay (includes neurological deficits related to procedures, treatments or investigations)_

The nurse reviewers examined the chart for evidence that the patient had developed a new neurological deficit during the index admission that was not present on admission and was unresolved at the time of discharge. Note that neurological deficits not directly related to procedures or investigations were triggered under trigger #9.

Examples given in the Operations Manual for trigger #10 included:

1. Post anaesthetic laryngeal nerve palsy
2. Following a series of post-operative injections in right buttock the patient developed weakness in right leg due to damage to the sciatic nerve.
3. Post elective carotid endarterectomy, patient developed dense hemiplegia, CT showed large cerebral infarct.
Trigger #11: Unexpected death

The nurse reviewer examined the chart for clinical or pathological evidence that the patient’s death was both unexpected and would not be considered a natural progression of the patient’s disease. All deaths without evidence of palliative care or where the patient died in the operating room or following completion of the surgery needed review for the cause. Nurse reviewers were advised to trigger in the following situations:

- Absence of definitive diagnosis
- Autopsy Report in data source
- Death during or following elective surgery
- Death despite resuscitation efforts
- Death within 24 hours of admission
- Death following an incident or accident
- Medical examiner’s Certificate
- Suicide
- Suspicious circumstances

The following were recommended not to be triggered:

- Any death that may have been considered to be a natural progression of the patient’s disease.
- Salvage surgery resulting in intra-operative or post-operative death e.g. emergent surgery in unstable trauma patient with severe head injury
- Death following advance care planning for palliative care

An example given in the Operations Manual for trigger #10 included:

1. Admitted in atrial fibrillation, high digoxin level, physician not notified, cardiac arrest one day post-admission, unable to resuscitate.
**Trigger #12: Inappropriate discharge to home/inadequate discharge plan for Index Admission (excluding “against medical advice”)**

The nurse reviewers were instructed to look for evidence that the patient was clinically unstable at time of discharge (e.g. febrile (> 38°C) within 24 hours prior to discharge, poor healing of surgical wounds, not passing urine/ flatus/ stools, no bowel sounds, not tolerating prescribed diet, analgesics not given orally). This did not include diseases in which any of the above was a symptom or condition related to the patient’s underlying disease and had been accounted for at the time of discharge (e.g. “Patient has been advised that fever will persist for up to 12 days”).

Examples given in the Operations Manual for trigger #12 included:

1. Discharged with red surgical wound red, temperature on day of discharge 38.2, readmitted with wound infection.

2. Patient admitted for lumbar decompression. Post-operative pain was controlled by intramuscular morphine which was ceased on the day of discharge. There is no evidence that the patient was reviewed by the pain management team. The patient was readmitted one day later with uncontrolled pain.

**Trigger #13: Cardiac/Respiratory arrest (successful)**

The nurse reviewer looked for evidence that the patient suffered a cardiac or respiratory arrest and was successfully resuscitated (at least temporarily). Evidence included any event associated with a respiratory rate of zero and endotracheal intubation or a heart rate of zero and chest compressions/epinephrine administration, or insertion of an external pacemaker. A cardiac or respiratory arrest occurring intra-operatively or in the post anaesthesia care unit, or in the first 24 hours post-operatively was
considered a trigger. A sudden cardiac arrhythmia with a resulting arrest code was not necessarily associated with an adverse event, but a failure to rescue due to lack of recognition of physiologic change in signs and symptoms was an adverse event. If the patient did not survive then the event was triggered under trigger #11.

Examples given in the Operations Manual for trigger #13 included:

1. Post lung biopsy became profoundly cyanotic, respiratory arrest, 3 litres blood loss from thoracic drains. Recent haemoglobin level was 5.7, no assessment performed.

2. Admitted unconscious to ED, admitting diagnosis intoxicated, cardiac arrest, CT scan showed extensive subdural hematoma.

*Trigger #14: Injury related to abortion or labour and delivery*

The nurse reviewers were instructed to look for evidence of an obstetrical mishap or complication of abortion, labour or delivery during the index admission or related to the index admission. Although most obstetric cases would have been excluded from the sample an injury related to a caesarean section requiring transfer to an acute public hospital may have been included. In these cases relevant antenatal and post-natal records were reviewed by the nurse reviewer. Events affecting the neonate were not included. Gynaecological procedures relating to pregnancy which involved injury were included.

Examples given in the Operations Manual for trigger #14 included:

1. Appendectomy resulting in a spontaneous abortion.

2. Post caesarean section, urine draining from vagina, fistula requiring surgical repair.
3. Post evacuation of retained products of conception developed severe breathlessness, admitted to hospital, lung scan showed pulmonary embolus.

*Trigger #15: Hospital acquired infection/sepsis (excluding infections/sepsis occurring less than 48 hours after admission)*

The nurse reviewer reviewed for evidence that the patient had acquired a nosocomial infection during the index hospitalisation. In order to qualify for this trigger the hospital acquired infection must have developed after a minimum of 48 hours in hospital. Infections may have been localized or systemic and may or may not have had concomitant microbiology confirmation. If acquired during index admission, the reviewers checked for evidence of an invasive procedure, breech in aseptic technique, administration of prophylactic antibiotic pre-operatively, or any delay in treatment. Included scenarios were: abscesses, central line infections, nosocomial infections, pneumonia confirmed in ICU, sepsis, surgical site infection, urinary tract infection, ventilator associated pneumonia and wound infections. Note that colonisation with MRSA or VRE in the absence of evidence of infection was not considered a trigger.

Examples given in the Operations Manual for trigger #15 include:

1. Elective Aortic Valve Replacement - post-op sternal incision red with drainage, required sternal debridement and packing.

2. IV cannula site from recent admission red with evidence of cellulitis, admitted for antibiotic therapy.
Trigger #16: Dissatisfaction with care documented in the medical record and/or evidence of complaint lodged (including documented complaint, conflict between patient/family and staff, discharged against medical advice)

The evidence for this trigger included any documentation that the patient or the patient’s family was dissatisfied with the care the patient received during the index admission. This included documentation of a complaint, conflict between the patient/family and staff or discharged against medical advice.

Examples given in the Operations Manual for trigger #116 included:

1. “Patient’s brother angry because of extubation and comfort measures only being instituted.”

2. Nursing notes state, “the patient is very angry that repeat X-Rays were required because the first series were lost.”

Trigger #17: Documentation or correspondence indicating litigation, either contemplated or actual

Evidence of this trigger included correspondence from a hospital administrator, attorney, patient or relative suggesting that litigation was pending or contemplated. The chart may have contained correspondence from a patient, a lawyer, or an indemnity insurer, suggesting the patient was dissatisfied with the quality of care or had suffered an injury or disability as a result of healthcare management. The record may have “LEGAL” stamped on it or be stored separately outside of the medical record department. Insurance claim documentation was not included in this trigger.

Examples given in the Operations Manual for trigger #17 included:

1. Letter from lawyer indicating that the patient has suffered a long-term injury due to fall out of bed occurring while in hospital for index hospitalisation.
2. Patient admitted for routine surgery. Intraoperatively the patient sustained a burn on his buttock from the diathermy plate requiring skin grafting. A solicitor's letter was filed in the clinic notes indicating legal proceedings were being undertaken.

*Trigger #18: Any other undesirable outcomes not covered above*

The nurse reviewer was instructed to use this trigger to report any complications or questionable outcomes not addressed by other criteria particularly those involving acts of omission.

Examples given in the Operations Manual for trigger #18 included:

1. Failure or delay in treatment of pneumonia in immunosuppressed patients

2. No record of bowel management for 10 days. Patient developed an acute bowel obstruction requiring surgical decompression.
Appendix 13: INAES Operations Manual adverse event variables and MCC categorisation

System-related factors

- Defective equipment or supplies
- Equipment or supplies not available
- Inadequate reporting or communication
- Inadequate training or supervision of doctors or other personnel
- Delay in provision or scheduling of services e.g. tests, x-rays, follow-up
- Inadequate staffing
- Inadequate functioning of hospital services e.g. pharmacy, blood bank, housekeeping
- No protocol or policy or failure to implement protocol or plan
- Lack of teamwork
- Patient factors e.g. non-adherence
- Inadequate discharge planning for continuity of care
  - Failure to educate patient including use of protocols e.g. asthma, congestive heart failure, diabetes etc.
  - Failure to assess patient immediately pre-discharge e.g. status, medications, mobility etc.
  - Failure to show evidence that discharge status was appropriate to home conditions educate e.g. care plan
  - Failure to communicate with Family Doctor
  - Failure to liaise adequately with community care staff
  - Failure to ensure patient’s environment was safe
  - Failure to adequately educate caregiver
  - Failure to communicate with child and family services (or equivalent in jurisdiction under review)
  - Failure to adhere to follow-up plan including repeat visits
**Diagnostic events**

Diagnostic events included incorrect or delayed diagnoses. This might have involved failure to use a recommended test or a delay in taking action following a diagnosis. The physician reviewer was instructed to select all that apply from the following list:

- Unavoidable diagnostic error despite reasonable diagnostic efforts
- Failure to obtain adequate history &/or physical examination
- Failure or delay to employ indicated test
- Inappropriate or outmoded tests used
- Test was incorrectly performed
- Test was incorrectly reported
- Failure or delay to act on results of tests or findings
- Failure to draw sensible/reasonable conclusions or make differential diagnosis.
- Failure or delay to get expert opinion from senior team member
- Failure or delay to get expert opinion from clinical specialist
- Failure or delay to get expert opinion from non-clinical specialist
- Expert opinion incorrect
- Delay in diagnosis
- Physicians or other professionals practicing outside area of expertise or beyond level of competence (specify)
- Other (specify)

**Surgical-related events**

Surgical events were the result of surgery and/or occurred within the first 30 days post operatively. The surgery must have been performed either during or before the index admission. The reviewer was instructed to select the most significant event and any other problems that were surgery related from the list below:

- Anastomotic Breakdown
• Anatomy - difficulty defining
• Bleeding – Major (2 units blood required)
• Bleeding – Minor (<2 units blood required)
• Cerebrovascular Accident (CVA)
• Complimentary alternative medicines
• Congestive Heart Failure (CHF)
• Deep Vein Thrombosis
• Infection – Other e.g. pneumonia
• Infection – Surgical Site
• Myocardial Infarction
• Organ damage - Inadvertent
• Perforation
• Pulmonary Embolus
• Rash
• Technical problem
• Wound Problem – other (e.g. dehisce)
• Wrong Patient
• Wrong Procedure
• Wrong Side
• Wrong Site
• Other events or comments (specify)

Next the reviewer indicated if any of the following problems were present, more than one could be selected:

• No apparent process of care contributed to the AE
• Adequacy of informed consent e.g. alternatives to procedure
• Delay in treatment
• Inadequate monitoring/supervision of patient after procedure
• Inappropriate or outmoded therapy used (specify)
• Inefficacious procedure – failed to relieve symptoms
• Patient inadequately prepared before procedure
- Patient inadequately sedated
- Physicians or other professionals practicing outside area of expertise or beyond level of competence (specify)
- Poor or failed communication
- Surgical Injury
- Wait times excessive
- Unable to determine (UTD)
- Other (specify)
- Any other performance error (specify)

**Fracture-related events**

Fracture-related events were the result of a fracture with or without surgical intervention. The fracture must have occurred and been managed either during or before the index admission. The reviewer was asked to indicate the location of the fracture and the nature of the fracture–related event:

- Re-operation – ‘re-do’ or re-operation of a previously performed surgery. For example, if following surgery to stabilize a fracture, the patient experiences no relief of symptoms or continues to have significantly reduced range of motion (ROM) requiring repeat surgery
- Prosthesis failure – for example if a patient undergoes a total hip replacement and is discharged to rehab. Within 9 months the patient is no longer able to weight bear on the operative side. Investigation reveals the prosthesis is loose and need to be replaced
- Operation-related – the event is associated with the surgery to manage the fracture
- Non-operation-related – the event is associated with the non-operative healthcare management of the fracture
- Other
**Anaesthesia-related events**

This is when the adverse event was related to the delivery of anaesthesia. The reviewer was asked to indicate the source of the adverse event and the most significant event from the lists below:

Source of adverse event:

- No apparent source
- Anaesthetic agent complication
- Equipment failure
- Intubation
- Monitoring during procedure – e.g. lack of or inefficient monitoring of the patient during surgery by the anaesthetist
- Pre-op assessment – if the adverse event related to information obtained from an inaccurate pre-operative assessment

Most significant event:

- Airway difficulty – laryngospasm
- Aspiration
- Hypotension
- Rash
- Vomiting
- Other events or comments

**Obstetric-related events**

Although cases with obstetric principal diagnoses were excluded the sample could include cases which were associated with an obstetric event if their principal diagnosis was non obstetric, e.g. readmission for treatment of a wound infection after a caesarean section. The physician reviewer indicated the stage (antenatal, delivery, post-partum) at which the event occurred and the mode of delivery (vaginal, instrument assisted, caesarean section).
**Medical procedure-related events**

This category was selected if the event was the result of a non-surgical medical procedure (i.e. procedures not performed in an operating room, e.g. bronchoscopy, cardiac catheterisation). The options to select for more detailed information were the same as those under surgical-related events.

**Drug-related events**

Drug (i.e. medication)-related injury included complications arising from errors and side effects of drugs. The reviewer was required to indicate the main therapeutic group of the implicated drug (e.g. anti-asthmatic, antibiotic, anticoagulant, etc.) and provide the generic name of all medicines involved in the incident. The most important and other contributing factors were chosen from the list below:

- No underlying cause (other than patient’s response)
- Allergic Reaction
- Delay in administering
- Delay in Prescribing
- Drug-Drug interaction
- Inadequate monitoring
- Problem with written drug order
- Rash
- Wrong dose
- Wrong drug
- Wrong duration of therapy
- Wrong route
- Wrong time
- Other (specify)
**Fluid-related events**

Intravenous fluid-related events included complications arising from the type of fluid, volume given and side effects. The reviewer was required to indicate the most important and other contributing factors to the fluid injury based on the list below:

- No Underlying Cause (other than patient’s response)
- Delay in Administering
- Fluid Volume Deficiency
- Fluid Volume Excess
- Inadequate Monitoring
- Wrong Dose
- Wrong Duration of Therapy
- Wrong Fluid
- Other (specify)

**Therapeutic adverse events**

Events in this category were the result of a clinical management event not already captured – including inappropriate or delayed treatment and failure to monitor care appropriately. The only information collected in this category was the free text description and system issues. Examples of this category of event provided in the Operations Manual were:

- Failure to take note of ‘routine’ observations, e.g. vital signs, neurological assessment, fluid balance
- Delay in noting laboratory or other investigation results, not aware of significance of results, failure to act appropriately on results
- Poor note-keeping
- Inadequate handover
- Lack of liaison with other staff
- Inadequate ‘out-of-hours’ cover/working practice
- Guideline/ protocol failure (either not available or not followed)
- Apparent failure to recognise deterioration
- Deterioration recognised but additional care not provided – “Failure to Rescue”
- Failure to recruit help
- Refused to attend

Adverse events not covered elsewhere

This category included resource issues and events classified as accidents, e.g. falls or burns. The only information collected in this category was the free text description and system issues.
**Major Clinical Categories**

- Blood, blood-forming organs or Immune disorders
- Circulatory system
- Conditions originating in the Perinatal period
- Digestive system
- Ear or mastoid process
- Endocrine, nutritional or metabolic disease
- External causes of morbidity or mortality e.g. Fall
- Eye and adnexa
- Genitourinary system
- Infectious or parasitic disease
- Injury, poisoning or other consequence of an external cause - e.g. Burn
- Mental or behavioural disorder
- Musculoskeletal system or connective tissue
- Nervous system
- Pregnancy, childbirth or the puerperium
- Respiratory system
- Skin or subcutaneous tissue
- Symptoms, signs or abnormal clinical or laboratory findings, not elsewhere classified
- Other
## Appendix 14: INAES STROBE checklist

STROBE Statement—checklist of items that should be included in reports of observational studies

<table>
<thead>
<tr>
<th>Item No.</th>
<th>Recommendation</th>
<th>Thesis section</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title and abstract</strong></td>
<td>1</td>
<td>(a) Indicate the study's design with a commonly used term in the title or the abstract</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Provide in the abstract an informative and balanced summary of what was done and what was found</td>
<td>Summary</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Background/rationale</td>
<td>2</td>
<td>Explain the scientific background and rationale for the investigation being reported</td>
<td>Introduction 1.7</td>
</tr>
<tr>
<td>Objectives</td>
<td>3</td>
<td>State specific objectives, including any pre-specified hypotheses</td>
<td>Introduction 1.8, methods 3.1</td>
</tr>
<tr>
<td>Study design</td>
<td>4</td>
<td>Present key elements of study design early in the paper</td>
<td>Introduction 1.2.2, 1.7, Methods 3.3</td>
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<tr>
<td>Setting</td>
<td>5</td>
<td>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection</td>
<td>Methods 3.7-3.12</td>
</tr>
<tr>
<td>Participants</td>
<td>6</td>
<td><em>(a) Cohort study</em>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</td>
<td>Methods 3.7-3.9</td>
</tr>
<tr>
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<td></td>
<td><em>Case-control study</em>—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</td>
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<td><em>Cross-sectional study</em>—Give the eligibility criteria, and the sources and methods of selection of participants</td>
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<td></td>
<td></td>
<td><em>(b) Cohort study</em>—For matched studies, give matching criteria and number of exposed and unexposed</td>
<td>Not applicable</td>
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<tr>
<td></td>
<td></td>
<td><em>Case-control study</em>—For matched studies, give matching criteria and the number of controls per case</td>
<td></td>
</tr>
<tr>
<td>Variables</td>
<td>7</td>
<td>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable</td>
<td>Methods 3.4, 3.13 Event type, preventability and impact groupings determined by previous</td>
</tr>
</tbody>
</table>
For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.

<table>
<thead>
<tr>
<th>Data sources/ measurement</th>
<th>8*</th>
<th>Methods 3.13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias</td>
<td>9</td>
<td>Methods 3.11, 3.12.6</td>
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</tbody>
</table>

Reduced reviewer bias with group training, study manual and structured web-based data entry. Assessed rater reliability using kappa.

<table>
<thead>
<tr>
<th>Study size</th>
<th>10</th>
<th>Methods 3.83</th>
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</thead>
<tbody>
<tr>
<td>Quantitative variables</td>
<td>11</td>
<td>Methods 3.13</td>
</tr>
</tbody>
</table>

Age analysed as a mean and 10 year increments.

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<thead>
<tr>
<th>Statistical methods</th>
<th>12</th>
<th>Methods 3.13</th>
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<tbody>
<tr>
<td>(a) Describe all statistical methods, including those used to control for confounding</td>
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<tr>
<td>(b) Describe any methods used to examine subgroups and interactions</td>
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<tr>
<td>(c) Explain how missing data were addressed</td>
<td>Not applicable</td>
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</tbody>
</table>
(d) **Cohort study**—If applicable, explain how loss to follow-up was addressed

*Case-control study*—If applicable, explain how matching of cases and controls was addressed

*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

<table>
<thead>
<tr>
<th>Results</th>
<th>Participants</th>
<th>13*</th>
<th>(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</th>
<th>Results 4.1</th>
</tr>
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<tbody>
<tr>
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<td></td>
<td>(b) Give reasons for non-participation at each stage</td>
<td>Results 4.1</td>
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<td>(c) Consider use of a flow diagram</td>
<td>Results 4.1.3</td>
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<table>
<thead>
<tr>
<th>Descriptive data</th>
<th>14*</th>
<th>(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders</th>
<th>Results 4.1.4</th>
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<td></td>
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<td>(b) Indicate number of participants with missing data for each variable of interest</td>
<td>Not applicable</td>
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<td>(c) <strong>Cohort study</strong>—Summarise follow-up time (e.g., average and total amount)</td>
<td>Follow up time was the period over which the</td>
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<td>Section</td>
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<td>Description</td>
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<tr>
<td>Outcome data</td>
<td>15*</td>
<td><strong>Cohort study</strong>—Report numbers of outcome events or summary measures over time\n\n<strong>Case-control study</strong>—Report numbers in each exposure category, or summary measures of exposure\n\n<strong>Cross-sectional study</strong>—Report numbers of outcome events or summary measures</td>
<td></td>
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<tr>
<td>Main results</td>
<td>16</td>
<td>(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included\n\n(b) Report category boundaries when continuous variables were categorized\n\n(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period</td>
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<tr>
<td>Other analyses</td>
<td>17</td>
<td>Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses</td>
<td></td>
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</tbody>
</table>

chart was reviewed – 12 months on either side of the index admission

Results 4.4-4.10

Results 4.4

Results 4.6

Results 4.10

Sensitivity analyses using difference adverse event criteria.
Confidence intervals provided for cost sensitivity analysis.

| Discussion | Key results | 18 | Summarise key results with reference to study objectives | Results 4.12 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | Discussion 5.10 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | Discussion 5.8 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | Discussion 5.11 |

| Other information | Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | Acknowledgements |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Adverse Events in Healthcare: learning from mistakes
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Word count (excluding references): 2416

Abstract

Large national reviews of patient charts estimate that approximately 10% of hospital admissions are associated with an adverse event (defined as an injury resulting in prolonged hospitalisation, disability or death, caused by healthcare management). Apart from having a significant impact on patient morbidity and mortality, adverse events also result in increased healthcare costs due to longer hospital stays. Furthermore, a substantial proportion of adverse events are preventable. Through identifying the nature and rate of adverse events, initiatives to improve care can be developed. A variety of methods exist to gather adverse event data both retrospectively and prospectively but these do not necessarily capture the same events and there is variability in the definition of an adverse event. For example, hospital incident reporting collects only a very small fraction of the adverse events found in retrospective chart reviews. Until there are systematic methods to identify adverse events, progress in patient safety cannot be reliably measured. This review aims to discuss the need for a safety culture that can learn from adverse events, describe ways to measure adverse events, and comment on why current adverse event monitoring is unable to demonstrate trends in patient safety.

Introduction

Traditionally performance in hospitals has been measured using routinely reported health data. Nevertheless, these data failed to identify patient safety concerns and shortcomings in care at Mid Staffordshire Foundation National Health Service (NHS) Trust. The inquiry by Sir Robert Francis into the trust found that the focus on targets and financial reporting to multiple bodies occurred to the detriment of patient care and staff wellbeing.¹ The Francis report highlighted the need for a patient-centred culture with the ability to collect, report, and analyse patient safety information.¹ However, in order to be able to evaluate safety performance, accurate and standardised data are required— including the systematic measurement of adverse events.²

Adverse event rates have been calculated in many different ways using a variety of data sources including patient charts, incident reporting, electronic databases, interviews of clinical staff, and examination of patients. Existing voluntary reporting collects only a small proportion of adverse events (around 1-10%) which are not representative of all adverse events (70% of those reported are falls, pressure ulcers and drug-related events whereas these constitute only 26% of adverse events detected by case note review).³ However the definition of an adverse event can vary widely, for example a patient safety incident in the National Health Service is defined as ‘any unintended or unexpected incident which could have or did lead to harm for one or more patients receiving NHS-funded healthcare’; thereby including incidents that result in no harm and also near misses.⁴ In comparison, the Harvard Medical Practice Study’s methodology used in retrospective chart review
studies in several countries, considers adverse events to be injuries resulting in prolonged hospitalisation, disability or death, which are caused by healthcare management; thereby encouraging collection of more severe events. These large international reviews of patient charts estimate that between 4% and 17% of hospital admissions are associated with an adverse event and a significant proportion of these (one to two thirds) are preventable. (Figure1) 

Research in hospitals in London and Scotland demonstrated adverse event rates of approximately 10%. Older patients and those with multiple co-morbidities are at higher risk of suffering an adverse event. A systematic review of eight chart review studies (from the United States, Australia, the United Kingdom, New Zealand and Canada) found a median overall incidence of adverse events of 9.2% (of which approximately 43% were preventable), with over half being operation (40%) or drug (15%) related. In the majority of adverse events a surgical service was providing the care at the time the adverse event occurred (the median proportion across the studies was 58% for surgical compared with 24% for medical services). Although most adverse events resulted in little or no disability, a significant minority (median 14%) caused permanent disability (7%) or death (7%).

![Figure 1: International incidence of hospital adverse events](image)

**Figure 1** International incidence of hospital adverse events

**A systems approach and a safety culture that learns from adverse events**

In healthcare, adverse events occur within a complex socio-technical system. An adverse event is not necessarily the result of one person making a mistake at the frontline of healthcare; rather conditions in the system often enable the adverse event to occur. A systems approach assumes humans are fallible and errors are inevitable. Such an approach identifies the prevalence and nature of adverse events so that when errors are made, the apparent causes and underlying factors
are reviewed to generate ideas for system improvements. Systems are therefore designed for safety, making it difficult for adverse events to occur whilst mitigating the ones that do happen. In this way errors are detected and corrected before harm is caused. Nevertheless, healthcare systems around the world have been slow to learn. An example is the continuing fatalities from intrathecal vincristine despite multiple reports, enhanced drug labelling, protocols and equipment modifications.

The systems approach requires a shift from a blame culture which incentivises people to cover up, to an ethos of safety management in the context of a just culture to maximise the potential to avoid future adverse events. A just culture reflects the balance between no blame and accountability, with the latter being needed to successfully implement safety strategies through individuals being accountable for their role within a safety system. The aviation industry is often held as an exemplar in terms of an industry that was able to change its culture and markedly improve safety with confidential reporting of near-misses providing a rich source of data from which safety lessons can be learned. However, healthcare is a significantly more complex system and represents a broader challenge with barriers including paucity of safety champions and leadership, individual clinician autonomy competing with teamwork, and multiple opportunities for communication breakdown.

The Francis report into Mid Staffordshire called for ‘fundamental culture change’ with person centred patient care, and openness. Its recommendations are not new – since 1999 government publications and safety investigations have advocated a national focus on patient safety, learning from failures and changing to a safety culture. The challenge of compliance with targets diverting focus from safer systems highlighted in the Francis report has also been demonstrated in qualitative research with other NHS hospitals, which found that clear organisational goals and leadership in patient safety are associated with greater patient satisfaction.

**Reason to collect adverse event data**

The occurrence of an adverse event has a number of detrimental effects on both patients and healthcare workers including physical and/or psychological harm, a loss of trust in the healthcare system, and reduced staff morale. Adverse events are associated with prolonged hospitalisation and are therefore expensive with additional societal costs in terms of reduced productivity and poorer population health. In the United Kingdom longer hospital stays due to adverse events are estimated to cost the government over £2 billion per year. The impact of adverse events on healthcare workers is an important consideration with staff often described as the “second victims” of adverse events.

Investigation of adverse events provides information on incidence and can demonstrate areas of risk and preventability that are amenable to action. Ideally, measurement of adverse event rates over time should be able to evaluate whether improvements are occurring. Local adverse event data may also highlight patient safety issues that require addressing at an organisational or local level as well as drive national policy. For example, in Canada, the publication of their first national adverse events study helped to launch the Canadian Patient Safety Institute.

**Measuring adverse events**
There is no gold standard for measuring adverse events, although retrospective chart review employing the Harvard Medical Practice Study approach is the standard methodology used in a number of international studies. This approach involves a two-stage chart review with nurses initially screening patient notes for ‘triggers’ from a list of scenarios that may indicate an adverse event has occurred (e.g. unplanned admission to intensive care, unexpected death, etc) followed by physician review of ‘triggered’ charts for any adverse event using a standard definition.

The global trigger tool (GTT) was developed by the US Institute for Healthcare Improvement as a less labour intensive method of chart review to identify adverse events. The first phase utilises a larger list of triggers than the HMP5 but limits reviewing to 20 minutes. Next, a physician assesses that potential adverse event only, not the entire record. A small number of charts are reviewed at each interval enabling change to be tracked over time. Using a broader definition of adverse events the GTT has identified higher rates of adverse events than the Harvard methodology (20-30%). However, in a direct comparison with the same criteria for defining adverse events the HMP5 method was found to be slightly more sensitive. In the future, automation of the global trigger tool with the electronic health record may enhance its utility for healthcare organisations.

Prospective collection of adverse events involves researchers or clinicians at the clinical interface identifying events as they occur. This may entail any combination of chart review, electronic searches, interviewing patients and staff, direct observation on the ward, and clinical examination of patients. Prospective methods identify similar numbers of adverse events as retrospective chart review (70% and 66% of total adverse events respectively in one comparative study) but these are not necessarily the same cases indicating that the true adverse event rate is probably higher than either estimate alone. Retrospective chart review does not impact on clinical work, yet it relies solely on the documentation available. Thus it can be difficult to judge preventability and may not be optimal for assessing the impacts of interventions to reduce adverse events or system factors responsible for particular events. Prospective adverse event determination, with less recall bias, aids assessment of preventability and studying system factors but is an additional task for frontline staff. These methods can also be used cross-sectionally though this has been found to elucidate fewer adverse events. Consistency between reviewers is a challenge for all chart review studies and standardised reviewer training and computerised data entry have been recommended as ways to increase inter-rater reliability.

Existing electronic data (e.g. admission or discharge clinical coding, private healthcare billing data) may be searched for adverse events with the benefits of being able to assess large numbers of patients/admissions and compare across different healthcare settings. However, this data (usually collected for other purposes) is dependent on the accuracy of the diagnostic coding system and limitations of the coding dictionary and has been found to have relatively poor sensitivity and specificity for adverse event identification. To improve the utility and standardisation of electronic search methods the Agency for Healthcare Research and Quality (AHRQ) developed a list of diagnostic codes that are indicators of adverse events. Preliminary work adapted some of these for use with NHS admissions data. The study found that admissions with these codes had higher mortality, length of stay and readmission rates. There was however, substantial variability between trusts and it is not clear whether this was due to variations in secondary diagnosis coding or quality of care. This method has been criticised for low sensitivity and may be better for case finding rather than quality of care reporting. Future adverse event determination is likely to involve a
combination of electronic data searching (especially with the advent of electronic health records and greater availability of clinical coding) alongside chart review.  

**Lack of consistent measurement of adverse events hampers progress**

A major barrier to progress in the field of patient safety appears to be the lack of reliable information on adverse events.  

Despite the multitude of methods described above to identify adverse events there is no internationally agreed measurement strategy with the ability to identify and analyse adverse events and monitor the impact of safety improvement programmes.  

Following Mid Staffordshire the National Advisory Group on the Safety of Patients in England called for measures of harm to be reported but exactly which ones remains to be established; whilst the Francis report specifically recommended mandatory reporting of all incidents involving patient harm.  

More importantly though, is the need to move from unsystematic methods such as voluntary reporting to coordinated systematic measurement. This could involve a combination of several methods including national audits, screening programmes (e.g. screening samples of patients for adverse drug events), and annual reviews of patient charts.  

Implementation of the electronic health record could also provide an opportunity to launch healthcare sector wide standardised reporting.  

Nevertheless in order to provide systematic measurement of adverse events, patient safety tools must be built in to electronic databases using knowledge of the local context to inform development and implementation.  

Furthermore, process improvement alone will not be sufficient to change culture and any such initiatives will require leadership at all levels of the healthcare system.  

The lack of systematic adverse event measurement and reporting is likely to have contributed to the absence of clear evidence of an overall reduction in adverse events.  

Whilst there have been some successes in specific areas of healthcare delivery (e.g. prophylaxis of venous thromboembolism, hospital acquired infections, post operative complications) using evidence-based strategies and robust measuring systems, reviews of overall adverse event rates have shown mixed results.  

Mortality and adverse event-related cardiac surgery deaths appear to have decreased over recent years although there has been no trend in reduction in adverse drug events.  

An analysis of data from the Medicare Patient Safety Monitoring System found reduced adverse event rates for patients admitted with acute myocardial infarction and heart failure (in particular for adverse events related to infections and medications) but not for those admitted with pneumonia or for surgery between 2005 and 2011.  

Another study using the global trigger tool to track adverse events across ten American hospitals over a 6-year period did not find any significant change in the rate of harm over time.  

**Conclusion**

Twenty years on from the first retrospective chart review studies, patient safety and quality are an accepted part of healthcare delivery but there remains a lack of consensus on how to collect and measure adverse events. This has meant progress is difficult to quantify. The system, therefore, has a limited ability to learn from its mistakes. In order to achieve (and monitor) healthcare sector improvements in patient safety we must plan for, and implement, (inter)national, standardised, and systematic measurement of adverse events alongside a sustained focus on a culture of safety in all
areas of healthcare delivery. Only once this is occurring can we effect whole system change and observe overall impacts on patient care.

Funding

Dr Rafter is funded through a grant from the Health Research Board of Ireland.

Conflict of interest The authors are undertaking the first Irish National Adverse Events Study, funded by the Health Research Board of Ireland within the Research Collaborative in Quality and Patient Safety.

References


due to variation in inclusion criteria for eligible events. We therefore also wished to examine how the Irish rate would vary with application of different published adverse event criteria.3 9 10 Patient data from 2009 were collected as it predated the establishment of the National Clinical Programmes in Ireland in 2010: the programmes aim to improve and standardise the quality of patient care.2 NAES was therefore designed to assess the baseline burden of adverse events and enable future evaluation of the effect of these programmes on patient safety. The INAES also employed web-based electronic data capture which has the potential to make the methodology more accessible for organisations to assess and monitor their patient-safety initiatives.

METHODS
To allow international comparison, we based our methods on the Canadian Adverse Events Study which employed a modified protocol of the Harvard Medical Practice Study.1 12 Similar protocols have been used in other international adverse event studies.2 4 9 13–26 29 This involves a two-stage review of patient charts with nurse reviewers screening for triggers that may identify an adverse event (stage 1), followed by physician reviewers determining the presence of adverse event(s) in trigger positive charts (stage 2).

Definitions
An adverse event was defined as an unintended injury or complication resulting in disability at the time of discharge, prolonged hospital stay or death and that was caused by healthcare management rather than by the underlying disease process.1 Disability was restricted to temporary (lasting up to a year) or permanent impairment of physical function.12 Healthcare management included the actions of individual hospital staff as well as the broader systems and care processes of healthcare, including both acts of omission (failure to diagnose or treat or manage) and acts of commission (incorrect diagnosis or treatment).12

Study sample
The study hospitals were all acute public hospitals in the Republic of Ireland—public hospitals provide approximately 88% of the national acute hospital beds.27 Thirty hospitals listed in the Irish Health Service Executive (HSE) 2012 hospital Casemix annual budget adjustment were invited to participate (this excluded eight hospitals with a sole clinical specialty focus, ie paediatrics, maternity and orthopaedics).28 Casemix is a system which groups patient data to compare activity and costs between hospitals.29 Hospitals were classified as ‘large’ if total annual inpatient, day case and emergency department Casemix units were over 100 000 and/or the hospital hosted a National Cancer Centre (ie, where staff with specialist cancer expertise are concentrated30); with the remainder classified as ‘small’. The approximate number of annual Casemix units (and distribution into inpatient/day case/emergency) for the nine large hospitals was 980 000 (22%/57%/41%), and for the 21 small, it was 860 000 (30%/23%/47%).28 Eighteen hospitals agreed to participate; six refused and six did not reply despite several contacts. The selection process involved random sampling of participating hospitals, stratified by health system (HSE) region and hospital size, to select eight hospitals: one ‘large’ and one ‘small’ from each of the four regions.31

After hospital selection, a random sample of 300–400 admissions (‘index admissions’) for the calendar year 2009 was generated at each site using the hospital’s local Hospital Inpatient Enquiry (HIEE) electronic discharge database. HIPE collects demographic, clinical and adminstrative information on discharges and deaths from acute hospitals in the Republic of Ireland. Discharge diagnoses and procedures are coded using ICD-10 AM/AHII/ACS 6th edition (International Classification of Diseases 10th revision Australian Modification/Australian Classification Health Interventions/Australian Coding Standards).32

The sampling frame included all inpatient admissions for patients aged at least 18 years who had a minimum stay in hospital of 24 h (or died within 24 h) and excluded admissions with a principal diagnosis related to obstetrics or psychiatry (ICD-10 codes F00-F99 and O29-092(73)). Admissions that were recorded in HIPE as being a transfer from another hospital were excluded as the likelihood was that full clinical information from the transferring hospital would not be available. Nurse reviewers conducted a further eligibility check prior to commencing review of each chart to identify ineligible admissions that were not able to be excluded using our HIPE methodology, that is, inpatients who were discharged within 24 h and obstetric admissions resulting in uncomplicated births with non-obstetric principal diagnosis codes. Early pregnancy (<20 weeks) was included in line with the Canadian Adverse Events Study.12

Reviewer training
Six nurse reviewers, each with a minimum of 7 years’ nursing experience and all having experience in clinical research, audit, hospital management and/or education and three physician reviewers (two recently retired respiratory physicians and one public health medicine physician) performed the chart reviews. Researchers from the Canadian adult and paediatric adverse events studies conducted face-to-face training of the reviewer group over 2½ days.12 17 An operations manual containing the study protocol and instructions for the web-based data collection was adapted from the Canadian manual. The Canadian website data entry forms and database were modified
for the Irish healthcare setting. The web-based data collection tool captured all study data. It had several advantages—prepopulation of admission demographic data, streamlined data entry (compulsory demographic fields, review of each injury with automatic adverse event determination if the definition was satisfied), enhanced data security (direct download to a secure server), central monitoring of site progress, automatic assignment of reliability charts and direct transfer into statistical software. Structured implicit review assisted physician reviewers to assess causation and preventability with the tool guiding reviewers through a series of questions before they made their judgements.

Reviewers independently reviewed 20 training charts immediately following the group training. These were assessed for inter-rater reliability by calculating the $\kappa$ statistic (nurse $\kappa=0.16$, physician $\kappa=0.52$). The low $\kappa$ for the nurses was due to a subset of nurses being oversensitive and triggering nearly all of the charts. The training charts were discussed in the reviewer groups before beginning data collection. The nurses had support on their initial 10 study charts. A 10% sample of patient charts was reviewed by all nurse or physician reviewers at each site. The $\kappa$ statistics in the field improved to nurses $0.79$ (95% CI 0.68 to 0.88) and physicians $0.59$ (95% CI 0.37 to 0.79).

A sample of trigger-negative charts at each site was also reviewed by a physician reviewer for adverse events as part of a sensitivity analysis of the stage 1 trigger methodology. The sensitivity and specificity were calculated as 96% and 64% respectively, with a 1.0% (95% CI 0.1% to 3.7%) prevalence of adverse events in missed charts (2/196 trigger-negative charts contained events).

Data collection
Patient charts were reviewed between December 2013 and January 2015. Stage 1 involved nurse review of each chart using a list of 18 ‘triggers’ (eg, unplanned readmission, hospital-acquired infection, adverse drug reaction; online supplementary appendix 1). Chart reviews centred on the index admission and all documentation 1 year before and after. The majority of patient charts were paper based or scanned paper records. In some sites, reports or correspondence were available electronically but these tended to duplicate documents included in the paper chart. There was no limit on time taken to review charts.

Stage 2 involved physician review of triggered charts to determine whether an adverse event had occurred. One physician reviewed each chart. Adverse events, which occurred within 12 months before, or during, the index admission, which were detected either during the index admission or within 12 months afterwards, were included. The physician reviewer rated the impact of the event, the likelihood that it was caused by healthcare management and its degree of preventability using standard scales (see online supplementary appendix 2). For each event, the physician classified its nature (ie, whether it was related to diagnosis or other clinical management, an operation or non-surgical procedure, a fracture, an anaesthetic, administration of fluids or medication, pregnancy and/or another type of event) and whether a system issue was involved (ie, if failures within the healthcare system contributed to the event). A consultant surgeon was available for advice on surgical cases.

Demographic and administrative data on the index admissions (age, sex, discharge diagnoses and procedures, consultant specialty code, admission and discharge dates) were collected at the time of random selection at each site. National demographic data for equivalent adult inpatients in acute public hospitals during 2009 was provided by the Healthcare Pricing Office and generated using the same HIPE search strategy as employed in the INAES sampling (see online supplementary appendix 3).

Analysis
Power calculation
A sample size of 1500 admissions was calculated using a 20% rate of adverse events and ±2% precision (with precision improving at lower rates). This allowed a precision of ±5% in any subgroup constituting 20% or more of the total sample. Thus, at least 187 eligible admissions were required to be reviewed at each hospital.

Weighting and analyses
The risk (period prevalence) of adverse events in inpatient hospital admissions was calculated as the proportion of admissions associated with one or more adverse events.12 The incidence density was calculated as the number of adverse events occurring per 100 admissions, excluding events occurring prior to the index admission (to avoid double counting). CIs for binary variables were modelled using logistic regression; CIs for incidence were calculated using Poisson regression with robust variance estimation to account for overdispersion; $p$ values were derived from logistic regression, unless otherwise noted. To maximise the number of adverse events reviewed, the sample was stratified such that half of admissions had undergone a surgical procedure (without stratification, this figure was approximately one quarter).16 The procedure codes for general anaesthetic, regional and neuraxial blocks (ACHI 9251400-9251499, 9250800-9251299) were used as proxies to indicate that surgery was likely to have been performed during the admission. Analyses were weighted for this sampling frame (ie, the ratio of admissions with and without the anaesthetic procedure codes in each hospital’s eligible study population). Inter-rater reviewer reliability was analysed using Cohen’s $\kappa$, with CIs calculated using a bootstrap method implemented in the user.
written command kapji. All analyses were performed using Stata release 13.1.

The national cost of adverse events in adult inpatients was estimated as the product of (1) the estimated number of adverse events—using the INAES incidence density of adverse events applied to the number of adult inpatient admissions to acute public hospitals in 2009, excluding those with obstetric and psychiatric principal diagnoses (n=319,844); and (2) the average cost of an event—calculated as the INAES mean number of added bed days attributed to adverse events multiplied by the average cost of an inpatient hospital bed in Ireland in 2009 ($909 per day).

RESULTS
A total of 2600 admissions were randomly selected from the hospitals’ HIPE discharge databases. Oversampling was performed to account for missing charts or ineligible admissions. Hospitals were advised to retrieve charts in batches from the top of the randomly generated list. Nurse reviewers were asked to review a target of 190-200 eligible charts at each site, reviewing the top 200 charts first and using the oversample as backup. A total of 1854 charts were screened for eligibility by the nurse reviewers and 1609 (87%) were eligible for the study (figure 1). The majority of ineligible admissions had a hospital stay of under 24 h. After excluding charts with inadequate documentation, 1580 admissions underwent a full stage-1 review (188-201 admissions per hospital), of which 6 were excluded by physician reviewers leaving a total of 1574 fully reviewed charts (figure 1).

The reviewed charts were comparable with national acute public hospital admissions in 2009 for age, sex and length of stay (see online supplementary appendix 3). However, a lower proportion of the national admissions compared with the INAES sample died during the admission (2.7% vs 4.8%, respectively). This is likely due to INAES excluding admissions with a hospital stay under 24 h unless the patient died, whereas the national figure includes all short-duration admissions.

A total of 45% of charts reviewed in stage 1 were trigger positive. The triggers of hospital-acquired infection, unplanned return to the operating theatre and unplanned removal/injury during surgery had the highest relative risks for subsequent adverse event determination (5.3, 4.8, 4.7, respectively; online supplementary appendix 1).

In stage 2, physician reviewers identified 247 adverse events in 211 admissions, including 15% with more than one event (see case descriptions in online supplementary appendix 4). Most (72.4%) of the adverse events occurred during the index admission (table 1). Approximately a quarter of events (23.5%) were detected after the index admission, and in 27%, the event occurred prior to the index admission.

The overall adverse event prevalence (ie, the proportion of admissions associated with one or more adverse events) was 12.2% (95% CI 9.5% to 15.3%) after weighting for the sample frame. The weighted incidence density was 10.3 adverse events per 100 admissions (95% Poisson CI 7.5 to 13.1). The mean age of patients was significantly higher among admissions with an adverse event than those without (61.8 years vs 55.4 years; p<0.001 (t test)), and with each 10-year age increment, there was an 18% increase in risk of an adverse event (OR 1.18, 95% CI 1.09 to 1.27). There was no difference in risk between women and men (p=0.693).

Of the 247 adverse events, 179 (72.5%) were judged to be preventable (see online supplementary appendix 2). When these results were adjusted for the sampling strategy, 72.7% (95% CI 58.8% to 83.3%) of events were deemed preventable (table 2), including 74.6% (95% CI 60.2% to 85.1%) of the 187 events occurring during the index admission. There was no difference between large and small hospitals in risk of an adverse event (p=0.918) or in the proportion rated as preventable (p=0.254).

Two-thirds (67.6%), weighted of adverse events resulted in no physical impairment or disability at discharge or in minimal-to-moderate impairment with recovery within 6 months (see online supplementary appendix 2). Nonetheless, 9.9% of the adverse events resulted in permanent disability, and 6.7% (occurring in 14 patients) were judged to have contributed to the
Table 1  The weighted distribution of adverse events by the timing of occurrence and detection

<table>
<thead>
<tr>
<th>Weighted distribution (95% CI) of all study adverse events*</th>
<th>Timing of adverse event occurrence (O) and detection (D)</th>
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<tbody>
<tr>
<td>48.9% (40.7% to 57.0%)</td>
<td>Before index admission D</td>
</tr>
<tr>
<td>27.7% (19.9% to 37.0%)</td>
<td>Index admission D</td>
</tr>
<tr>
<td>23.5% (18.1% to 29.9%)</td>
<td>After index admission D</td>
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</table>

*Point estimates and CIs were weighted to account for the sampling frame.

The patient’s death (see online supplementary appendix 2). There was no significant difference in risk of death in admissions that had adverse events compared with admissions without events (p=0.331).

Patients who experienced adverse events had a median length of index admission of 7 days (IQR 3, 17) compared with four days (IQR 2, 8) without adverse events (p<0.001, Wilcoxon–Mann–Whitney). Physician reviewers judged events occurring in the index admission to result in a mean of 6.1 (95% CI 4.8 to 7.7) additional hospital days in that admission or readmission(s). This represents an additional cost of approximately €555.00 for each adverse-event-associated admission, which when extrapolated nationally gives an estimated annual cost of hospital-based adverse events to the Irish healthcare system of €194 million.

Adverse event risk was higher in admissions with anaesthetic procedure codes indicating a surgical procedure was likely to have occurred, than in admissions without these codes (17.9% (95% CI 13.5% to 22.3%) versus 10.2% (95% CI 7.2% to 13.1%)). However, when the 1499 admissions with medical or surgical consultant specialty codes were compared, there was no difference in event frequency between the specialties: medical-weighted prevalence 11.9% (95% CI 8.3% to 15.5%), surgical 13.1% (95% CI 9.8% to 16.5%). The type of adverse event varied by specialty, with surgical specialties having a greater proportion of operation-related events (occurring during surgery or within 30 days postoperatively), whereas therapeutic events (inappropriate or delay in treatment or failure to monitor) and medication-related events were the dominant categories for medical specialities (see online supplementary appendix 3). A system issue was identified in 106 events (weighted proportion 46.1% (95% CI 31.5% to 61.4%)). Overall, adverse events resulting from errors of omission were as common as those resulting from errors of commission (data not shown), with no significant difference between medical and surgical specialties (p=0.627).

Adverse event prevalence varied significantly if different criteria were used to identify the events (table 3). For example, exclusion of events occurring in the index admission and discovered subsequently reduced the weighted risk to 9.4% (95% CI 7.4% to 11.9%). Similarly exclusion of events prior to the index admission resulted in a risk of 8.6% (95% CI 6.7% to 10.9%). If events caused by healthcare management outside the index hospital were included (eg, occurring in general practice, nursing homes or other healthcare facilities), then the weighted prevalence rose to 14.6% (95% CI 11.6% to 18.3%). Furthermore, using a lower threshold to determine likelihood of causation by healthcare management (a score of ≥2, online supplementary appendix 2) increased the prevalence to 14.5% (95% CI 11.3% to 18.4%), and if events caused by healthcare

Table 2  Adverse event frequency, by hospital type

<table>
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<tr>
<th>Variable</th>
<th>Hospital type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Small</td>
</tr>
<tr>
<td>Number of admissions sampled</td>
<td>792</td>
</tr>
<tr>
<td>Number of admissions associated with an adverse event</td>
<td>108</td>
</tr>
<tr>
<td>Crude adverse event prevalence (95% CI)</td>
<td>13.6% (11.4% to 16.2%)</td>
</tr>
<tr>
<td>Weighted adverse event prevalence (95% CI)*</td>
<td>12.4% (7.7% to 17.1%)</td>
</tr>
<tr>
<td>Number of adverse events</td>
<td>123</td>
</tr>
<tr>
<td>Number of incident adverse events (ie, excluding events occurring prior to the index admission)</td>
<td>89</td>
</tr>
<tr>
<td>Crude incidence of adverse events per 100 admissions (95% CI)</td>
<td>11.2 (9.0 to 13.8)</td>
</tr>
<tr>
<td>Weighted incidence of adverse events per 100 admissions (95% CI)*</td>
<td>9.5 (7.0 to 11.9)</td>
</tr>
<tr>
<td>Weighted percentage of adverse events that were preventable (95% CI)*</td>
<td>80.1% (68.7% to 91.5%)</td>
</tr>
</tbody>
</table>

*Point estimates and CIs were weighted to account for the sampling frame.
In contrast, adverse events were reported in only 1.9% of patient contacts in 2011 to the National Incident Management System (NIMS). 37, 38 While not directly comparable (NIMS includes near-misses and community settings), there appears to be significant under-reporting of adverse events in the Irish healthcare system, similar to other research. 7, 22 Reasons for this include lack of awareness or belief in the value of reporting, fear of litigation and lack of a supportive culture encouraging reporting. 39, 40

The leading categories of events by frequency in INAES were similar to other studies: operation related, therapeutic, medication related and diagnostic. Additional analyses will be needed to delineate the nature of events within these categories for prioritisation of future patient-safety initiatives. Unlike the Canadian study, we did not find a difference with hospital size; however, hospital categorisation differs between studies and necessarily relates to local demographic and health service factors. 15 Over 70% of INAES adverse events were considered preventable. This appears high (compared with a previous systematic review aggregate estimate of 43.5%) but preventability is likely to increase over time with advances in surgical techniques, therapies, quality initiatives and increased availability of documentation with electronic clinical notes; 32, 33 more recent studies have reported similar rates. 16, 18, 22 Furthermore, judgement of preventability can only be based on available documentation and will be influenced by reviewers’ experience and knowledge. 42, 44 In line with other research, undergoing a surgical procedure was associated with a greater risk of an adverse event. 14 However, this finding was not true for the surgical specialties overall. This is probably because a quarter of admissions coded with a

**Table 3** Weighted occurrence of Irish National Adverse Events Study (INAES) adverse events with the application of international adverse event eligibility criteria

<table>
<thead>
<tr>
<th>Adverse event eligibility criteria</th>
<th>Weighted prevalence (95% CI)</th>
<th>Weighted incidence density (95% CI)</th>
<th>Magnitude (%) change in prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Include only events related to the index hospital (exclude events caused by healthcare management outside the index hospital) with healthcare management causation at least more likely (≥2 out of 6, online supplementary appendix 2). INAES prevalence</td>
<td>12.2% (9.5% to 15.5%)</td>
<td>N/A*</td>
<td>Baseline</td>
</tr>
<tr>
<td>Exclude adverse events detected after the index admission</td>
<td>9.4% (7.4% to 11.9%)</td>
<td>10.9 events per 100 admissions (8.2 to 13.7)</td>
<td>23% decrease</td>
</tr>
<tr>
<td>Include adverse events occurring prior to the index admission. INAES incidence</td>
<td>8.6% (6.7% to 10.9%)</td>
<td>10.3 events per 100 admissions (7.5 to 13.1)</td>
<td>30% decrease</td>
</tr>
<tr>
<td>Include adverse events in all settings (e. include events caused by healthcare management outside the index hospital)</td>
<td>14.5% (11.6% to 18.3%)</td>
<td>N/A*</td>
<td>20% increase</td>
</tr>
<tr>
<td>Include events with at least slight-to-moderate evidence for healthcare management causation (≥2 out of 6, online supplementary appendix 2)</td>
<td>14.5% (11.3% to 18.4%)</td>
<td>N/A*</td>
<td>19% increase</td>
</tr>
<tr>
<td>Include all events with at least slight-to-moderate evidence for healthcare management causation (≥2 out of 6, online supplementary appendix 2) in all settings.</td>
<td>17.0% (13.4% to 21.3%)</td>
<td>N/A*</td>
<td>39% increase</td>
</tr>
</tbody>
</table>

*Not applicable; unable to calculate an incidence because including events occurring in admissions prior to the index admission as well as events detected in subsequent admissions will result in double counting.
surgical speciality (ie, under the care of a surgical consultant for their principal diagnosis) did not appear to have had surgery (judged by the absence of a procedure code for an anaesthetics) while approximately 5% of those with a medical code underwent surgery.

Comparison of published adverse event rates is problematic. Results from international studies conducted over a 30-year period present the burden of adverse events at one point in time and may not reflect current practices or quality and patient-safety improvements in that healthcare system. In addition to differences in setting, these studies differed by eligible population, threshold for causation by healthcare management, extent of documentation reviewed and the timing and location of events relative to the index admission. For example, some studies included paediatric and all obstetric patients and had no length-of-stay eligibility criteria, some had a lower threshold for causation, while others did not include events that were discovered before, or after, the index admission.

When our data were recalculated by applying different adverse event criteria, the INAES prevalence varied from 8.6% to 17.0% (representing a 30% decrease to a 40% increase when compared with the main result of 12.2%). This highlights the challenges inherent in measuring and comparing adverse events. Current variation in methodology and definitions, as well as setting and year, make it difficult to assess whether there are intrinsic differences in adverse event occurrence between healthcare systems.

The cost of adverse events is significant in terms of adverse outcomes for patients and the trauma and consequences for all involved—patients, families and staff. Financially, an annual cost of €1394 million represents approximately 4% of the Irish healthcare acute services 2009 budget. This is an underestimate as it does not take into account costs such as escalation of care and litigation. Furthermore, day cases, emergency department assessments, paediatric and the majority of obstetric and psychiatric admissions were not included in our study.

Study limitations
Not all invited hospitals agreed to participate. However, the INAES included large and small hospitals from across the country and was comparable with national demographic data. Our estimate may not have captured all adverse events. For example, the two-stage methodology means that not all charts undergo physician review. However, our trigger screening sensitivity analysis indicates that the adverse event rate would only result in a relative 4% increase (to 12.7%) if physicians had reviewed all charts. Events detected in the index admission that occurred over a year beforehand (estimated to contribute 10% of all events), and events from the index admission that were detected after a year are not included. In addition, retrospective chart review is restricted to chart documentation without direct information from staff involved in patient care. Our reviewers commented that there was significant variability across hospitals in terms of filing practices, recording of information (extent of documentation, handwritten or typed), layout of drug charts, presence of discharge summaries and availability of investigation results. Furthermore, studies comparing prospective and retrospective methodologies have found that although these methods identify similar rates of events, they do not necessarily identify the same adverse events.

In addition, chart review relies on consistency between reviewers, in order for physicians to agree that an adverse event has occurred, all three elements of the definition (injury, resulting disability at discharge/prolonged hospitalisation/ death and causation) must concur. Our x² statistic of 0.59 for physicians is in line with other studies, where rs have ranged from 0.25 to 0.78. This need for reviewer consistency across elements of the adverse event definition highlights the problem of rater reliability in detecting adverse events. To enhance reviewer consistency, INAES employed standardised training and structured explicit review, with the data collection tool guiding physicians to informed professional judgements.

Irish healthcare has undergone extensive change due to the economic recession and the growth of the quality movement, including the National Clinical Programmes. Therefore, our study of adverse events in 2009, near the start of these dual influences, provides an important baseline and the opportunity to link safety with subsequent organisational reform. However, while our results describe the burden of adverse events, the retrospective methodology may be viewed as a blunt instrument for monitoring specific quality initiatives, as adverse events are a heterogeneous group. A reduction in one category may be counterbalanced by an increase in others, leading to no overall change in adverse event rates. Thus, interventions to reduce adverse events need to be targeted at specific adverse event categories, and studies monitoring effects tailored accordingly.

The INAES web-based tool is now available for use in Irish hospitals, providing an electronic application for chart review that will allow hospitals to conduct their own reviews and monitor patient-safety initiatives. The results from these reviews will be directly comparable with the INAES results. Furthermore, other national studies have spearheaded the development of national patient-safety organisations and policy, and we anticipate that this study will further support patient-safety initiatives in the Irish healthcare setting.

CONCLUSION
INAES provides the first estimate of adverse event occurrence within the Irish healthcare system and an important measure of the burden and impact of these
events. Our results give an overview of the types of patient-safety issues that will help guide future interventions to reduce specific adverse events and improve safety. We found a significant discrepancy between our rate of adverse events and that reported to the national reporting scheme. Therefore, efforts must be made to encourage a ‘reporting culture’. From an international perspective, this most recent large-scale retrospective chart review national study shows broad consistency yet again in the frequency and nature of adverse events. Patient-safety experts should question why, after 50 years, there has been so little evidence of overall improvement.

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Contributors NR: design, acquisition of data, analysis and interpretation of the data and drafting of the manuscript. DW and AH: design, reviewed analysis and interpretation of the data and critical revision of drafted manuscript. RM: design, analysis and interpretation of the data and critical revision of drafted manuscript. SC: design, acquisition of data, interpretation of data and critical revision of drafted manuscript. GW, POC and DV: design, interpretation of data and critical revision of drafted manuscript. All authors approved the final version of the article.

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