Delayed presentation to the Emergency Department following a head injury: current care and the risks of intra-cranial pathology.

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Abstract

**Background:** Head injury is a common reason for Emergency Department attendance. The clinical dilemma is differentiating between patients who have mild/minor head injuries into those that can be discharged following clinical review and those that require a CT head scan to rule out neurosurgical pathology. Clinical decision rule research to aid this risk assessment has been conducted almost exclusively on patients presenting within twenty-four hours of injury. Delayed presentation head injury patients may be a distinct sub-population with a different risk profile.

**Methods:** Three studies were undertaken. A systematic review was conducted to identify and assess existing evidence regarding the risk assessment in delayed presentation head injury patients. A survey of emergency physicians using clinical vignettes was used to assess variation in the investigation of this patient group. Lastly, six months of audit data were analysed to assess the size of the population of delayed presentation head injury patients, and the use and sensitivity of existing NICE guidelines in their risk assessment.

**Results:** Few existing studies of poor methodological quality were found. A large degree of variation in clinical practice was identified in the investigation of this group. Head injury patients presenting after twenty-four hours of injury were found to account for 15.5% of CT head scans for the investigation of adult head trauma. In patients presenting after twenty-four hours of injury 30% of identified intra-cranial injuries were in patients without a NICE indication for a CT head scan compared to only 2.2% of intra-cranial injuries in patients presenting within twenty-four hours of their injury.

**Conclusions:** Head injury patients presenting more than twenty-four hours after injury represent a significant clinical sub-population. A different approach to that recommended in the current NICE guidelines may be required in the risk assessment of this group.
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Author’s Declaration:

I confirm that this work is original and that if any passage(s) or diagram(s) have been copied from academic papers, books, the internet or any other sources these are clearly identified by the use of quotation marks and the reference(s) is fully cited. I certify that, other than where indicated, this is my own work and does not breach the regulations of HYMS, the University of Hull or the University of York regarding plagiarism or academic conduct in examinations. I have read the HYMS Code of Practice on Academic Misconduct, and state that this piece of work is my own and does not contain any unacknowledged work from any other sources. I confirm that any patient information obtained to produce this piece of work has been appropriately anonymised.
Chapter 1

Introduction

This introductory chapter outlines the background to the management of Emergency Department head injury presentations in the UK. In particular it outlines how clinical decision rule research has been used to address the problem of deciding which of these patients requires computed tomography (CT) imaging and which can be safely discharged following assessment with advice. It highlights the limitations of this research in regard to the risk assessment of delayed presentation head injury patients and why this group of patients may be a distinct sub-population.

Incidence of head injury

Head injury is a very common presentation to the Emergency Department (ED). There are approximately 1.4 million resultant attendances annually to the ED in England and Wales. Between a third and a half of these are in patients aged under sixteen and 95% of these attendances are for minor head trauma (NICE, 2014). Severity of injury is classified by the degree to which a person’s conscious level is impaired, as measured by the Glasgow Coma Scale (GCS). Patients with a GCS less than 13 following injury are in the moderate and severe categories (Miller, 1986). There is variation in the terminology used to describe patients with a GCS greater than or equal to 13 following an injury. Traditionally this group was described as having sustained a minor head injury (Miller, 1986). However, in North America the definition of a minor head injury also encompasses a loss of consciousness or disorientation following the injury (Stiell et al., 2001). Therefore the term “mild head” injury has been applied to those patients with a GCS of 13 or greater (NICE, 2014). For the purpose of this project the terms “mild” and “minor” head injury are used interchangeably to refer to patients with a GCS of 13 or greater following head injury.
Clinical consequences of head injury

Patients with moderate and severe head injuries as defined by the Glasgow Coma Scale are at high risk of death and serious intra-cranial pathology (Miller, 1986). However, the incidence of intracranial pathology clinically important enough to warrant hospital admission in mild head injury has been found to be in the range of 4.8% - 8% and in the UK it is estimated that only 0.2% of patients attending hospital with a minor head injury will die and 1% of patients will require neurosurgery (Albers et al., 2013, NICE, 2014, Stiell et al., 2001, Pandor et al., 2011). That said, the phenomenon of the patient with a minor head injury who “talks and dies” is an established clinical scenario (Kim et al., 2013). It characterises patients who deteriorate fatally, after a lucid period, following a head injury due to an expanding intra-cranial haemorrhage (Kim et al., 2013). This suggests that although the incidence of significant pathology is low in minor head injury patients, these injuries can be life threatening. The diagnosis and neurosurgical treatment of intra-cranial haemorrhage and other significant injuries can be life saving and the chance of success is time critical.

Emergency Department Investigation of Head Injury: The Clinical Decision Rules

A plain X-ray computed tomography scan of the head (CT head scan) has almost 100% sensitivity for detecting traumatic injury to the brain and skull fractures (NICE, 2014). It is the gold standard radiological method for investigating traumatic brain injury in the acute setting. However, a CT scan has several disadvantages: it has a relatively high radiation dose; it is expensive; and the use of the CT scanner for the investigation of minor head injuries has an opportunity cost in terms of its use in the investigation of other potential pathologies. Estimating the potential harm to an individual patient through the radiation exposure of a single CT head scan is difficult (Westra, 2014). Research to quantify this risk is on-going. We know that repeated exposure to radiation increases the risk of developing malignancy. The younger a patient, the higher
the associated radiation risk, due in a large part to the higher baseline lifetime risk of developing malignancy (Westra, 2014). Women are also at higher cancer risk from radiation exposure (Smith-Bindman et al., 2009). It has been estimated that 1 in 8100 women and 1 in 11080 men at age 40 who underwent a single non-contrast CT head scan would develop a resultant malignancy (Smith-Bindman et al., 2009). The paediatric population is particularly susceptible with the relative risk of brain tumours and leukaemia potentially being tripled in children exposed to levels of radiation comparable to that of a CT head scan, compared to other non-exposed equivalent children (Pearce et al., 2012). The absolute risk to individual patients remains very low, but if all 1.4 million annual head injury patients in the England and Wales were subjected to a CT head scan, there would be harmful effects in the population. The average cost of a CT scan is quoted as approximately £108 (Hull Royal Infirmary electronic ordering system April 2015). This is more than ten times more expensive than any X-ray. In addition, the CT scanner represents a finite resource, the use of which has to be balanced between the investigation of multiple potentially life-threatening pathologies and its associated radiation risk.

The clinical dilemma with minor head injuries therefore lies in identifying the small number within that population who have potentially life-threatening injuries without subjecting every patient to a CT scan. Various clinical decision rules have been developed to allow better targeting of CT head scanning to those at higher risk within this group and the safe discharge of the rest. Clinical decision rules are defined as “decision making tools derived from original research that incorporate three or more variables from the history, examination or simple tests” (Stiell and Wells, 1999). They are designed to allow clinicians to effectively determine the risk of a condition for a patient at the bedside in order to guide their further management. In adult populations with minor head injuries the two most used and validated rules are the New Orleans CT head rule and the Canadian CT head rule (CCHR). These form the basis of many international head injury guidelines as well as the current UK National Institute for Health and Care Excellence (NICE) guidance. Accordingly, practice in England and Wales is based upon the CCHR decision rule (NICE, 2014).
The New Orleans decision rule was derived from a study of 520 patients with a minor head injury, aged over 3 years, presenting within twenty-four hours of injury (Haydel et al., 2000). All of these patients had CT scans. Seven variables that are measurable either when taking the history or conducting the examination were found to correlate with a positive finding on a CT head scan. These 7 criteria were then prospectively validated against a further equivalent group of 909 minor head injury patients presenting to the ED. All of these patients underwent CT scanning and it was found that the presence of any of the 7 variables was 100% sensitive for the presence of abnormality on CT scan. Therefore the absence of all 7 variables had negative predictive value of 100%.

The Canadian CT head Rule (CCHR) is based on a prospective decision rule derivation study of 3121 patients presenting to the emergency department with a minor head injury (Stiell et al., 2001). In the study minor head injury was defined as blunt trauma to the head with an accompanying loss of consciousness, amnesia or disorientation in patients with a GCS of 13 and above. The cohort only included patients if the presentation had occurred within twenty-four hours of injury. Significantly, patients with focal neurological deficit, seizures or taking anti-coagulant medications were excluded. The primary outcome was the need for neurosurgery, which was defined as undergoing a neurosurgical procedure or death, within seven days of the injury. A secondary outcome measure was of “clinically significant findings on CT”. This represented a more selective radiological end point than in the New Orleans study. Twenty-four potential variables were evaluated against these outcomes. The presence of any one of seven factors were found to be predictive of a clinically significant abnormality on CT scan. The presence any one of five of these risk factors were found to be predictive of the need for neurosurgery and therefore defined as “high risk” clinical features.

The Canadian and New Orleans CT head rules were both externally validated shortly after their publication and were found to have 100% sensitivity for patients requiring neurosurgery (Smits et al., 2005). In this paper Smits also demonstrated
that the New Orleans decision rule had a higher sensitivity, and negative predictive value, for detecting traumatic findings on CT (97.7%, -99.4%) than the CCHR (83.4%, -87.2%). This was offset by a very small reduction in patients scanned (3% reduction in patients undergoing CT head imaging) when compared with the CCHR (37.3% reduction in patients undergoing CT head imaging). This is not surprising given the methods of the two studies and the more selective definition of clinically relevant CT findings used in the original CCHR study. The authors argued that missing a few findings on CT that did not require surgery was acceptable when balanced against the comparative reduction in CT scanning in the minor head injury population. This is the view adopted in the NICE head injury guidelines and it is the CCHR that underpins current practice in the CT head imaging of minor head injury patients in England and Wales (NICE, 2014).

In the original Canadian CT head rule study, Stiell et al (2001) identified five high risk factors and two additional moderate risk factors. The presence of any one of the high risk factors were found to put a patient at increased risk of having a neurosurgical outcome. The presence of either of the two moderate risk factors increased the risk of clinically significant pathology being identified by CT scan. The five high risk factors identified by the CCHR are as follows: GCS < 15 two hours following an injury; suspicion of an open or depressed skull fracture; signs of a basal skull fracture; greater than one episode of vomiting following the injury; and an age greater than or equal to 65 (Stiell et al., 2001). If any of these risk factors is present in a patient following a minor head injury the CCHR group recommends a CT scan be performed immediately (Stiell et al., 2001). The current version of NICE guidance regarding head injury recommends a CT head scan within one hour for a patient presenting with a head injury if any of the five high risk factors identified in the CCHR is present, apart from an age greater than or equal to 65 (NICE, 2014). Patients aged greater than or equal to 65 are recommended by NICE to have a CT scan if their injury has accompanying loss of consciousness or post-traumatic amnesia, but this CT scan can be deferred to up to 8 hours following the injury. This accords with the definition of head injury used by Stiell et al (2001), which was of blunt trauma to the head with accompanying loss of consciousness, amnesia or disorientation. In England and Wales therefore,
the other four risk factors trigger a CT scan in a larger population of patients than envisioned in the original paper by Stiell et al (2001).

The two moderate risk factors identified by Stiell et al (2001) were: the presence of one of four high-risk mechanisms for injury; or retrograde amnesia of more than thirty minutes prior to sustaining the injury. Presence of either of these risk factors is predictive of clinically important findings on CT but not of need for neurosurgery. In these circumstances the authors recommended either admission for observation or a CT scan. What was defined as clinically important omitted several findings on CT head scan, where the patient was neurologically intact. The CCHR derivation study defined clinically insignificant CT head findings as including: a solitary contusion smaller than 5mm in diameter; smear subdural haematomas less than 4mm in diameter; localised subarachnoid blood less than 1mm thick; isolated pneumocephaly; and closed depressed skull fractures not through the inner table of the skull (Stiell et al., 2001). The rationale is that these are radiological findings that would not require hospital admission. By contrast, the New Orleans group defined any traumatic finding on CT as their sole clinically important end point (Haydel et al., 2000).

What constitutes clinically important findings on CT following a head injury is debatable. The NICE guidelines for England and Wales state that any traumatic finding on CT is potentially clinically important (NICE, 2014). Indeed, some commentators would recommend hospital admission and observation for at least twenty-four hours for patients with a small isolated contusion or subdural haematoma, due to the risk of potential deterioration (Alahmadi et al., 2010). These two medium risk factors have been incorporated into the NICE head injury guidance (NICE, 2014). NICE recommends that a CT head scan should be performed within 8 hours of injury if either of these medium-risk factors is present along with a loss of consciousness or post-traumatic amnesia. The latter accords with the definition of minor head injury used by Stiell et al (2001).
The additional indications for a CT scan of the head following a head injury in current NICE guidelines include the presence of a clotting disorder or patient anti-coagulation, post traumatic seizure activity or a focal neurological deficit (NICE, 2014). The presence of any of these factors mandates a CT scan within one hour. Patients with any of these characteristics were excluded from the original Canadian CT head study on the basis that they were already established in clinical practice as indications for an immediate CT scan. The presence of anti-coagulation, especially due to warfarin, is a well recognised risk factor for intracranial haemorrhage. Elderly patients taking warfarin who have suffered a head injury have been shown to have a 8% risk of intracranial haemorrhage, compared to a baseline risk of 5.3% and a higher associated rate of mortality (Cohn et al., 2014). To reflect how significant this risk factor is, the latest NICE recommendation, based on a large systematic review, is that any patient currently receiving warfarin treatment, or with a history of a clotting disorder, who sustains a head injury should have a CT scan within 8 hours (NICE, 2014).

A prospective comparison of performance of NICE guidance with other decision rules in a population of patients presenting with a minor head injury, within twenty-four hours of injury, found it to be almost 100% sensitive for the detection of neurosurgical lesions and all traumatic findings on CT (Stein et al., 2009). The same paper indicated that all comparable decision rules achieved this degree of sensitivity, but that the application of NICE guidance involved scanning the greatest number of patients with a minor head injury for a very modest gain in detection of traumatic findings on CT. Additionally, the study found that there was no NICE indication for a CT head scan in 2 patients with intracranial bleeds from a total sample of 107. However, this comparison is slightly false as the strict application of the New Orleans decision rule and CCHR in this study excluded some higher risk sub-populations, like patients taking warfarin, in analysis that are accounted for by the NICE guidelines. A large UK based systematic review found the NICE guidelines to provide a cost-effective compromise between sensitivity and specificity when compared to other decision rules (Pandor et al., 2011).
NICE recommends the discharge of patients with normal CT head scans providing their GCS has returned to 15/15 and there are no other factors to warrant hospital admission (NICE, 2014). There is a recognised phenomenon of delayed intracranial haemorrhage, where despite a normal CT scan, a patient subsequently develops a bleed (Riesgo et al., 1997). The incidence of this phenomenon in anti-coagulated patients is reported as up to 1.1% for secondary intra-cranial haemorrhages that are severe enough to warrant neurosurgical evacuation (Cohn et al., 2014). Only 0.04% of the total head injury population are reported to have any type of secondary haemorrhage, irrespective of severity (Isokuortti et al., 2014). A large systematic review found that in a pooled sample of 62,000 GCS 15/15 head injury patients that had normal CT head scans following a head injury, only three subsequently deteriorated due to secondary intra-cranial haemorrhage (af Geijerstam and Britton, 2005). For GCS 15 patients, not taking anti-coagulants, it is accepted that a normal CT scan allows the safe discharge of head injury patients (Pandor et al., 2011). There is some debate about whether anti-coagulated head injury patients should be admitted or undergo repeat CT scanning due to their increased risk of secondary intra-cranial haemorrhage. There is a tendency to do this in North America (Cohn et al., 2014). In the UK there is variation in the admission of this population (Pandor et al., 2011). Overall, especially for patients not taking anti-coagulating medications, a normal CT head scan following a minor head injury makes the chance of developing further intra-cranial complications extremely unlikely.

Current practice in the management of minor head injuries in the NHS in England and Wales is therefore based on a modified version of the CCHR that allows this population of patients to be divided into those patients who are at low risk for significant intra-cranial injuries and can be discharged immediately, and those patients who require a CT scan. A negative CT scan will allow discharge providing the patient is otherwise well. The application of the clinical decision rules, and therefore the NICE guidelines, requires a trade off between sensitivity and specificity. It is necessary to identify all patients who require life saving neurosurgical treatment, but it is accepted that a small number of less important injuries can be missed in order to reduce the overall burden of CT imaging.
In Scotland equivalent SIGN guidelines are used to inform clinical-decision making regarding CT imaging of head injury patients (Scottish Inter-Collegiate Network Guideline, 2009). The current iteration of these guidelines is very similar to the NICE head injury guidelines used in England and Wales. However, they were only introduced in 2009 in Scotland and previously in Scotland clinical guidelines recommended more restrictive CT head imaging of minor head injury patients. Also, the 2009 SIGN guidelines differ from the current NICE head injury guidelines in that they emphasise persistent headache as an indication for CT imaging in GCS 15 head injury patients. They also recommend a more restrictive approach to CT imaging anti-coagulated head injury patients (NICE, 2014, Scottish Inter-Collegiate Network Guideline, 2009).

**Delayed presentation Head Injury Patients**

One sub-group of patients with minor head injury which current NICE guidance and the wider literature fails to address directly are those who present in a delayed fashion, specifically twenty-four hours after injury. The original derivation studies for both the New Orleans decision rule and the CCHR, on which NICE guidance is based, only sampled populations presenting within twenty-four hours of their head injury (Stiell et al., 2001, Haydel et al., 2000). Validation of the CCHR and NICE guidelines has only been in populations presenting within twenty-four hours of injury (Harnan et al., 2011, Smits et al., 2007, Smits et al., 2005, Stein et al., 2009, Fabbri et al., 2005, Kavalci et al., 2014). No studies have specifically assessed whether these decision rules can be applied to patients who present after twenty-four hours of injury. Why is this an important group? It has already been observed in the research literature that there is a paucity of studies on such patients (Barrow et al., 2012). This group potentially has delayed onset pathology and a different risk profile to those who present within twenty-four hours of injury.

Significantly, there is evidence that the majority of minor head injury patients with intra-cranial haemorrhage who deteriorate, do so within twenty-four hours (Reynolds et al., 2003, Choudhry et al., 2013). A large case series of 757 patients
with minor head injury and an intracranial bleed on a CT scan found that 87% who deteriorated did so within twenty-four hours of the injury and all patients who deteriorated did so within 62 hours (Choudhry et al., 2013). Therefore patients presenting after twenty-four hours following injury could be less likely to have intracranial haemorrhage or other pathology that requires neurosurgery. Indeed, when CT scanning was routinely less available in the UK, it was common practice to admit patients following a head injury, in lieu of a CT scan, for a period of observation up to twenty-four hours. The assumption was that any deterioration would occur within that time period. Patients with simple traumatic findings on CT head scan such as small contusions and small subdural haemorrhages are recommended to be admitted for a period of twenty-four hours in case of deterioration (Alahmadi et al., 2010). Patients presenting after twenty-four hours may therefore represent a more benign sub-population at less risk of deterioration and therefore significant pathology. Application of current CT head injury imaging guidelines may consequently cause over-investigation.

The delayed onset haemorrhage is an established, although rare, phenomenon. The decision rules were not derived with the intention of identifying this pathology. There is a case study of secondary of intra-cranial haemorrhage occurring six days after an initial head injury (Inamasu et al., 2001). This represents a distinct pathology, which although rare may prompt delayed presentation following a head injury. Patients taking warfarin or other anti-coagulants are at higher risk of developing delayed intracranial bleeds, but even the most conservative practice recommends admission of this group and with a repeat CT head scan undertaken at twenty-four hours (Cohn et al., 2014). Here again, the assumption is that after twenty-four hours the risk of deterioration is low. It has already been established that those who re-attend following a head injury are a high risk group for intra-cranial pathology (Voss et al., 1995). What is not known is whether this risk extends to entire population of patients presenting after twenty-four hours of injury.
Persistent symptoms following minor head injury are well characterised and form part of a spectrum of disease that can be defined as mild traumatic brain injury or the post-concussion syndrome (Cancelliere et al., 2012). The acute post-traumatic headache has been found to occur in up to two thirds of patients following a minor head injury. These headaches occur within 48 hours of the injury and have been found to last for a median of three days (Lieba-Samal et al., 2011). The symptoms of the post-concussion syndrome have been found to occur in up to 24% of patients following a minor head injury (Lannsjo et al., 2009). They include: persistent headaches; mood changes; fatigue; dizziness and difficulties with concentration (Cancelliere et al., 2012). The post-concussive syndrome usually lasts between three and 12 months following minor head injury (Cancelliere et al., 2012). There is debate within the literature regarding the definition and aetiology of the post-concussion syndrome (Rose et al., 2015). The presence of traumatic abnormality on a CT head scan following a head injury has not been found to predict development of symptoms of the post-concussive syndrome (Lannsjo et al., 2013). However the presence of the post-concussion syndrome may prompt delayed ED attendance following a head injury and the investigation of such symptoms with a CT head scan does not appear to be warranted if they do not predict the presence of clinically significant intra-cranial injuries.

Studies looking specifically at patients who present in a delayed manner following a minor head injury are few. A single abstract of a case series of 206 patients presenting after twenty-four hours following blunt head trauma reported an incidence of 6.3% of pathology found on CT (Borczuk, 1997). This is comparable to figures for patients presenting within twenty-four hours, but none of these patients required neurosurgery. The study by Borczuk (1997) was conducted prior to the advent of clinical decision rules so it is difficult to know how it relates to current practice. It does confirm the premise that patients with a minor head injury presenting after twenty-four hours may at a lower risk for neurosurgical intervention. A paper which defined delayed presentation as those presenting after 12 hours found that 194 patients out of 2900 patients presented within this time frame over a year long period (Hemphill et al., 1999). Furthermore, this paper found an incidence of traumatic CT findings in this group of 3.1% in those
scanned immediately and an overall incidence of 3.6% in those who re-presented and subsequently had a CT scan. This is a lower prevalence of traumatic intra-cranial injuries than quoted for those with minor head injury as a whole. The authors made no comment about how many of these patients subsequently had neurosurgery. They did observe that one patient re-presented having had a normal CT scan and died with a delayed intracranial haemorrhage. Again, this study was conducted before the widespread adoption of CT head decision rules and it is therefore difficult to relate to current practice.

A study which defined delayed presentation as those presenting after four hours, found 497 such patients in an 18 month period (Barrow et al., 2012). Usefully this paper was directly relevant to current UK practice. It found that those presenting after four hours had an incidence of 2.2% of any traumatic finding on CT head. This is lower than the prevalence of traumatic intra-cranial injuries in samples of minor head injury populations presenting within twenty-four hours (Stiell et al., 2001, Haydel et al., 2000). Application of current NICE guidance to this group presenting after 4 hours resulted in a similar proportion (29.6%) of patients receiving a CT scan as to those presenting within four hours, albeit with this lower yield rate (Barrow et al., 2012). The same study found that the proportion of patients who presented after four hours of injury that required neurosurgery to be similar to the proportion of patients that were found to require neurosurgery in previous studies conducted on populations presenting within twenty-four hours of injury (Barrow et al., 2012).

**Application of Current Guidelines to the Delayed Presentation Head Injury Population**

Currently, therefore NHS practice in England and Wales is based on the application of a clinical decision rule regarding the management of patients presenting to the ED following a minor head injury. This decision rule has not been validated in patients who present after twenty-four hours of injury. The
A proportion of patients who currently present after twenty-four hours of injury in England and Wales is not known. However, approximately 6.7% of patients with minor head injury have previously been found to present to hospital after 12 hours of injury (Hemphill et al., 1999). There is some evidence that this group may be at a reduced risk of deterioration compared with those that present within twenty-four hours. However, patients who re-attend have been found to be a higher risk group (Voss et al., 1995). Delayed intra-cranial haemorrhage is a rare but distinct pathology that may prompt delayed presentation to the ED. The New South Wales (NSW) head injury guideline state that patients who present in a delayed fashion following a minor head injury should be treated as higher risk as they are more likely to have unresolved symptoms (New South Wales Government Ministry of Health, 2012). Therefore patients who present after twenty-four hours may be a group where current guidance is less effective at risk stratifying patients with minor head injuries. Therefore, use of existing guidelines may risk either over-investigation, or conversely, missing important intra-cranial injuries when applied to this population.

Overview of The Research

There appears to be a paucity of research regarding the delayed presentation ED head injury population. It is unclear whether this group has a different prevalence, and therefore risk, of significant traumatic brain injuries identified by CT imaging. It is also unclear how current clinical decision-rule research can be applied to this group. This is particularly relevant to patients that present after twenty-four hours of injury as the most widely used decision rule, the CCHR, has only been validated in patients presenting within 24 hours of injury.

Aims:

The main aims of this project are to:
1) Compare the risk of clinically significant traumatic intra-cranial injury as identified by CT head imaging in a delayed, and non-delayed, presentation head injury patient population.

2) Assess whether delay in presentation affects the clinical application of NICE head injury guidelines and their ability to identify significant intra-cranial injuries.

These aims are achieved by undertaking three interconnected phases of this project:

Phase 1 (Chapter 2) is a systematic review of available research regarding the delayed presentation head injury population. It assesses current evidence regarding whether delay in presentation is associated with a lower risk of significant intra-cranial injury.

The second phase (Chapter 3) is a national clinical-vignette survey of ED physicians. The objective of this phase is to establish whether variation in clinical practices exists in the application of current NICE guidelines to delayed presentation minor head injury patients.

The third phase (Chapter 4) involves the analysis of six months of routinely collected data about head injury patients that attended Hull Royal Infirmary ED. Analysis is focused on head injury patients that have undergone CT head imaging as identified by the hospital electronic requesting system. Limited analysis of head injury patients identified by hand searching is also undertaken, but as discussed later, this was found to be unreliable data source. The objectives of the third phase of the project are to:

i) Assess what proportion of CT head scans for head trauma, and head injury attendances, are for adult patients presenting after 24 hours of injury.

ii) Compare the prevalence of significant intra-cranial injuries identified by CT imaging in adult head injury patients presenting within, and after 24 hours, of injury.
iii) Compare the adherence to, and the sensitivity of, the NICE head injury guidelines in adult head injury patients that have undergone CT head imaging presenting within, and after, twenty-four hours of injury.

iv) Assess the reasons adult head injury patients have for presenting after twenty-four hours of injury.

The first aim of this project is addressed in phase 1 and objective ii of Phase 3 of the research. The second aim of this project is addressed by phase 2 and objective iii of phase 3 of the research. Each phase of the project uses a different method to provide evidence about the current clinical management of head injury patients that present after a delay following a head injury and how their risk of serious injury may differ from other head injury patients. The different methods were chosen as they were the best available methods to address the specific objectives of each phase of the project, and therefore the overall research aims, within the available time and resources.

Chapter 5 presents a synthesis of findings and the implications of the completed research.
Chapter 2: The Systematic Review

This chapter will present the findings of a systematic review that was undertaken to determine whether delay in presentation following a head injury is associated with a reduced risk of significant intra-cranial pathology.

Background

As outlined in Chapter 1 there are approximately 1.4 million attendances to EDs in England and Wales following head injury each year (NICE, 2014). Ninety-five per cent of these attendances are patients with minor/mild head injuries, as defined by a GCS score of 13, 14 or 15 (Miller, 1986, NICE, 2014). Research has been directed at differentiation of patients with minor/mild head injury into two groups: those who are sufficiently low risk to be discharged on the basis of clinical history and examination alone; and those who require further investigation by CT head scan. NICE guidelines are used to facilitate this risk assessment in the UK. NICE guidelines are based upon the CCHR, which was derived in a population of patients presenting within twenty-four hours. The NICE guidelines and CCHR have both only been validated in populations of patients presenting within twenty-four hours of injury (NICE, 2014, Fabbri et al., 2005, Smits et al., 2007, Smits et al., 2005, Harnan et al., 2011, Stein et al., 2009, Kavalci et al., 2014).

Not all patients present to the ED immediately after sustaining a head injury, particularly if they fall into the minor/mild head injury group. Some present after twenty-four hours (Barrow et al., 2012). There is evidence that patients with a minor head injury and an intra-cranial haemorrhage who clinically deteriorate, do so within twenty-four hours (Choudhry et al., 2013, Reynolds et al., 2003). This suggests that patients presenting after this time, with signs and symptoms indicating minor/mild head injury, may be a selected sub-population at lower risk of significant intra-cranial pathology. However, there are case reports in the
literature of patients with delayed onset intra-cranial haemorrhage following a head injury (Ferrera and Mayer, 1997, Snyder and Salo, 1990), and the occurrence appears more likely in anti-coagulated patients (Cohn et al., 2014, Docimo et al., 2014). The Australian New South Wales (NSW) Health Guidelines identify patients who present in a delayed fashion as a potentially higher risk group (New South Wales Government Ministry of Health, 2012). The NSW guidelines acknowledge that this is based on a scant evidence base, but postulates that patients who present late have on-going symptoms and are therefore a self-selecting higher risk population. Furthermore, patients who re-present to the ED after an initial acute presentation following head injury have been identified as a high risk group (Voss et al., 1995). Re-attendance may be due to worsening or persistence of symptoms and consequently delayed presentation head injury patients may be at a similarly higher risk of significant intra-cranial injuries.

It is currently unclear whether delay in presentation to the ED after head injury is associated with a different risk of intra-cranial pathology. This has implications when applying existing guidelines to the risk assessment of patients with minor/mild head injury who have a delayed presentation. Therefore the systematic review portion of the project aimed to systematically identify and evaluate studies that measured whether the estimated incidence of traumatic intra-cranial injury in patients with head injury is affected by a delay in presentation.

Planning and Question Formulation

The systematic review question and protocol was developed iteratively involving consultation with an ED head injury specialist (WT). The PROSPERO register of systematic reviews was checked to ensure that a similar review was not already being undertaken. The UK-based NICE and SIGN guidelines were reviewed to ensure that a systematic review regarding delayed presentation head injury patients had not already been undertaken in the formulation of these guidelines. These guidelines made no direct reference to delayed head injury patients.
Given that current guidelines are based on studies of populations presenting within twenty-four hours and that the clinical dilemma of investigation of patients is exclusive to patients with minor/mild head injury the systematic review was initially planned to focus specifically on the population of patients with minor head injury who present after twenty-four hours. The first postulated systematic review question was “Does delay in presentation greater than twenty-four hours reduce the likelihood of intracranial pathology in minor head injury in the Emergency Department?” The “PICO” format would have been used to structure the question in the following way: The population of interest would have been patients with a mild/minor head injury presenting to the ED. The “intervention” would have been delay in presentation greater than twenty-four hours. The “comparator” would have been a population presenting acutely, within twenty-four hours. The primary outcome would have been of any traumatic findings on CT head and secondary outcomes would have been of death or neurosurgery. The ideal studies for inclusion would be large cohort studies. This would have provided summary statistics of relative risk or odds ratios that could have pooled in a meta-analysis to give an overall relative estimate of injury between groups.

A scoping search and background literature review indicated that there were likely to be very few studies that investigated delayed presentation head injury populations. The delay in presentation investigated was likely to be variable and not necessarily twenty-four hours. It also indicated that there were unlikely to be large cohort studies or studies that directly compared delayed presentation groups to non-delayed presentation groups. Limiting studies to those conducted on mild/minor head injury samples would also potentially under-estimate the incidence of injury. Presumably moderate/severe head injury patients that presented late may initially have had minor/mild head injuries and therefore limiting the inclusion criteria would fail to account for mild/minor head injury patients that clinically deteriorated.

The review title was therefore changed to “Does a delay in presentation to the Emergency Department affect the rate of intracranial pathology in patients
following a head injury? A systematic review.” The PICO model for systematic reviews is intended for reviews of interventional studies and ideally suited for framing questions that can be answered by meta-analysis of randomised controlled trials. The use of this model for this topic was therefore not ideal. However, for want of a better model, the population being studied would be all patients with head injury presenting to the ED in a delayed manner where delay would include any time period of delay as defined in a primary study. The “intervention” or more accurately exposure would be the delay in presentation. The incidence of clinical outcomes in delayed presentation populations would be compared to the incidence of intra-cranial injury and need for neurosurgery as widely established in patients presenting within twenty-four hours of injury. The primary outcome would remain any traumatic finding on CT head following head injury and secondary outcomes would be death or neurosurgery. It was determined that any study design apart from single case studies would be included. Towards the end of the systematic review process the title was refined slightly to, “The risk of a bleed after delayed head injury presentation to the ED: A systematic review.” This made the title more succinct without any changes to the protocol and methods.

Methods:

A key consideration in developing the protocol was the limited time and resources available to the team in undertaking the systematic review. The timescale was set to a six month period from November 2014 to April 2015. This limited the extent of the electronic search strategy planned and undertaken. However, the nature of the systematic review question precluded the conduct of randomised control trials (RCT) or controlled interventional trials because time of presentation of a patient following a head injury cannot be randomised or allocated. This made the electronic search of databases such as CENTRAL that only contain RCTs and interventional trials, less relevant. The fact that the authors anticipated finding only a few studies of variable quality and design being identified meant that meta-
analysis was unlikely to be possible. Accordingly only a narrative data synthesis was planned.

The PRISMA systematic review checklists were used in the formulation of the systematic review protocol, the conduct of the review and its reporting (Shamseer et al., 2015, Moher et al., 2010). The systematic review is currently registered on the PROSPERO prospective register of systematic reviews. The hyper link is: (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015016135). The protocol can be downloaded from the PROSPERO register and is available in appendix 1.

**Search Strategy**

Relevant terms related to delayed diagnosis, delayed presentation and intracranial pathology were identified after reviewing both the PubMed Pubreminer service (http://hgserver2.amc.nl/cgi-bin/miner/miner2.cgi) and Medical Subject Headings (MESH – via the US National Library for Medicine MESH browser at http://www.nlm.nih.gov/mesh/MBrowser.html). An electronic search strategy was devised aiming to capture all studies relating to patients presenting in a delayed fashion following a head injury. Articles of potential interest were identified from searches in MEDLINE (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present) and EMBASE (1974 to 2015 January 23) (Wolter Kluwers Health at http://ovidsp.uk.ovid.com/sp-3.13.1a/ovidweb.cgi). The full search strategy is attached in appendix 2.

Further studies of interest were identified through reference checking of full text articles retrieved by the electronic search strategy and by using the ‘related articles’ features of PubMed and Google Scholar. Further free-text searches of Google Scholar, PubMed and NICE Evidence Search (www.evidence.nhs.uk) were also undertaken. The UK based NICE and SIGN head injury guidelines had
already been identified as potentially relevant and these were identified through free text searches. NSW head injury guidelines had also been identified in the planning stage as having a specific section pertaining to delayed presentation head injuries and therefore this guideline was identified through a free text search. The bibliographies of these three guidelines were interrogated for studies of interest.

**Inclusion Criteria**

Studies had to be conducted in populations of patients presenting in a delayed manner to the ED following a head injury. As it was anticipated few studies would be identified, no specific time limit on delay was applied. However, included studies had to specifically evaluate a population of patients who had presented after a defined time delay. The time delay constituted the “intervention” and the ideal comparator would be to a sample of patients presenting in a non-delayed fashion. Again, because of the limited literature in this area, this comparator was not necessary for inclusion and comparison would be made to the established rate of intra-cranial pathology in patients with head injury presenting within twenty-four hours of injury. Included studies had to measure an outcome of traumatic intra-cranial pathology as identified by CT scan. A secondary outcome of death and need for neurosurgery was also included. Any study design, apart from single cases studies, were included.

**Study Selection**

Articles were considered for inclusion through a title and abstract review of papers identified from the electronic searches and by review of bibliographies and related articles by two independent reviewers (CM and CMS). NICE, SIGN and NSW head injury guidelines were scrutinised independently for pertinence and the reference lists of relevant material were reviewed for inclusion (NICE, 2014, New South Wales Government Ministry of Health, 2012, Scottish Inter-Collegiate Network Guideline, 2009). Studies for potential inclusion were identified and the
full-texts of these papers were obtained. Final inclusion of studies was determined against the eligibility criteria. Any uncertainty or disagreement was resolved after discussion between the two reviewers. Although in practice not necessary, where disagreement could not be resolved, it had been agreed that WT would be the final arbiter.

**Assessment of Methodological Quality**

It was initially thought that the systematic review search strategy would potentially yield cohort studies that compared the rate of intracranial injury in patients presenting in a delayed manner following a head injury to those who presented in a non-delayed fashion. Therefore it was envisioned that the Newcastle-Ottawa scale could be used to quality assess studies. However, no cohort studies were identified and the disparate and observational nature of the studies made it difficult to use an alternative formal quality assessment tool. Therefore a narrative critical appraisal of each paper was conducted instead. This critical appraisal was informed where relevant by the Cochrane handbook for assessing quality in observational studies (Reeves et al, 2011).

**Data Extraction and Synthesis**

Included studies were reviewed and variables relating to study population, design, outcome measures and results were extracted. An assessment of methodological quality was reported in a narrative fashion. Given the paucity of studies likely to be identified and actually included, a meta-analysis was neither planned nor undertaken. A narrative data synthesis was conducted.
Results

The MEDLINE and EMBASE search returned 419 potentially relevant articles. Eight were selected for full-text review (Docimo et al., 2014, Barrow et al., 2012, Hemphill et al., 1999, Snyder and Salo, 1990, Hamilton, 2010, Root J.D., 1993, Jones S., 2013, Hawley et al., 2013). Two of these studies met the criteria for inclusion into the systematic review (Barrow et al., 2012, Hemphill et al., 1999). Other search strategies identified two additional articles of interest and the full text of these studies was retrieved (Borczuk, 1997, Voss et al., 1995). One of these (identified from bibliography search) was included in the systematic review (Borczuk, 1997). This paper was an abstract. Multiple attempts were made to contact the author to ascertain whether the data had been published fully elsewhere. These attempts were unfortunately unsuccessful. The study selection process is presented below, in Figure 1.
Figure 1: Prisma Flow Chart
(modified from http://www.prisma-statement.org)

Records identified through database search strategy (n = 550 (131 duplicates))

Additional records identified through other sources (n = 2)

Total records (n = 421)

Records screened by title and abstract (n = 421)

Records excluded (n = 411)

Full-text articles excluded (n = 7)

Two case reports only
One referred to delayed onset of haemorrhage rather than delayed presentation
Two studies about missed diagnosis of intracranial haemorrhage
One study of "attenders" rather than delayed first presentation
One conference preceding of epidemiology of child head injury- the authors were contacted for the full paper

Full-text articles assessed for eligibility (n = 10)

Studies included in qualitative synthesis (n = 3)

Critical appraisal of each paper. Meta-analysis not feasible.
Data Extraction

The studies included in the systematic review are summarised in Table 1. Data extraction was undertaken to include: study design and methods; the population on which the study was conducted; the definition of delay in presentation and whether a comparator non-delayed presentation population was also included; all outcome measures and results reported; and a quality assessment of each paper. One reviewer (CM) undertook the initial data extraction. A second reviewer (CMS) then checked the data extraction against the original studies and made modifications. CM and CMS then met to agree upon the final data extraction outcomes.

One prospective observational English study (Barrow et al., 2012), one retrospective observational U.S. study (Hemphill et al., 1999) and a U.S. case series (abstract only) (Borczuk, 1997) were identified. None of these studies included non-delayed presentation comparator groups and so could not be defined as cohort studies. The studies defined delay in presentations as four (Barrow et al., 2012), twelve (Hemphill et al., 1999) and twenty-four hours (Borczuk, 1997) respectively. There was a large degree of heterogeneity in the populations on which the studies were conducted. Barrow et al 2012, included patients aged 17 years or older presenting with a GCS of 14 or 15. Hemphill et al 1999, studied patients of any age presenting with GCS 15. Borczuk et al 1997, included patients aged 16 years or older, but did not state the presenting GCS and only included patients who had undergone a CT head. The main outcome in all three studies was defined as any traumatic abnormality identified on CT head scan. This rate was found to be 2.2% (Barrow et al., 2012), 3.1% (Hemphill et al., 1999) and 6.3% (Borczuk, 1997).
## Table 1: Summary of Data Extraction

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Study Design</th>
<th>Outcome Measures</th>
<th>Results</th>
<th>Quality Appraisal</th>
</tr>
</thead>
</table>
| Barrow et al 2012 | Inclusion Criteria: Age ≥ 17 years  
- GCS 14 or 15 at presentation  
- Presenting to ED > 4 hrs. after injury | Prospective observational study  
NICE guidelines used to triage patients to CT head and discharge  
Data Collection: Daily identification of cases from search of paper records and review of computerised discharges | "Positive CT": Any traumatic finding related to presenting injury  
2-4 week telephone interview follow-up for further treatment/deterioration  
Identification of clinical risk factors predictive of intra-cranial injury | 497 patients included:  
- 193 presented 4-12 hrs.  
- 140 presented 12-24 hrs.  
- 62 presented 24-48 hrs.  
- 58 presented 24-168 hrs.  
- 44 presented ≥ 1 week  
147/497 (29.6%) had CT head; 64/147 presented 4-12 hrs, 50/147 12-24 hrs, 11/147 24-48 hrs, 21/147 48-168hrs, 1/147 > 1 week  
11/497 (2.21%) positive CT scans; 1/11 presented 4-12hrs, 3/11 12-24hrs, 4/11 24-48hrs, 3/11 48-168hrs  
4/497 (0.80%) had neurosurgery; 3/4 (75%) presented 12-48hrs after injury, 1/4 (25%) 48-168hrs  
1/497 died (0.20%) – time since presentation not reported  
69/497 (13.9%) contactable at 2 weeks; 11/69 (15.9%) symptomatic  
Lower rates of intra-cranial injury to previous studies  
Similar rates of neuro-surgery to previous studies  
Statistically significant predictors of intra-cranial injury: LOC, coagulopathy, evidence of injury above the clavicles, open or depressed skull fracture and acute alcohol/drug use | Prospective and contemporaneous review of notes - likely that most eligible cases were identified and included  
4 hours is not a long delay; may be comparable to a patient presenting immediately but with a long ED wait to be seen  
No control or comparison group.  
Sampling biases: small numbers, young population, > 50% from Indian subcontinent  
Small absolute rates of pathology, therefore prone to outlier bias.  
Very high loss to follow-up. |
### Table 1: summary of data extraction

<table>
<thead>
<tr>
<th>Hemphill et al 1999</th>
<th>Inclusion Criteria:</th>
<th>Retrospective chart review</th>
<th>Significant delayed injury. Defined as &quot;abnormal CT results such as: intracerebral bleeding, skull fracture, or subdural or epidural haematoma&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any age</td>
<td>Searched 85,000 ED charts</td>
<td>Comparisons between patients with / without CT</td>
</tr>
<tr>
<td></td>
<td>GCS 15 at presentation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presenting to ED &gt; 12 hrs. after injury</td>
<td></td>
<td>Comparisons between hospitals</td>
</tr>
<tr>
<td></td>
<td>Re-attenders included</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exclusions:</td>
<td>None stated</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Dual-site: academic Level I Trauma Centers (San Antonio, USA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan – Dec 1996</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**2,900 patients with head injury**

194 (6.69%) presented > 12 hours:

- 112/194 (56.9%) female
- 34±24 years (mean±SD)
- 21/194 (10.8%) re-attenders
- 101/194 (52.1%) patients had CT head; 9/21 (42.9%) of re-attenders had CT head

6/194 (3.1%) patients had abnormal CT scans:

- 2 infants (aged 1m and 5m)
- 4 adults (29F, 46F, 60M, 74M)
- Note: one patient (74M) presented GCS 3 with large DSH at 25hrs after normal CT acutely after injury – required neurosurgery and died
- 1 patient re-presented at three months with headache: chronic SDH – did not originally have CT head

Mean time to presentation:

- Overall: 73±105 hrs.
- If abnormal CT: 29.3±10.7 hrs.

### Borczuk et al 1995

**ABSTRACT ONLY**

**Inclusion Criteria:**

- Age > 16 years
- Presenting > 24 hrs.
- Blunt head injury
- Had CT head

**Exclusions:** None Stated

**Single-site over 2-years**

**Case Series**

Any abnormality on CT head

206 consecutive patients identified

GCS on presentation not stated

13/206 (6.3%) had abnormality on CT head

No patient required neurosurgery

**Case series**

Sampling biases: small numbers, only those had CT head after injury included

Abstract only – unable to contact authors for further information.

‘Abnormality’ on CT not defined
Key Limitations and Validity Assessment of Included Studies

Methodologically all the identified studies suffer from two key weaknesses. None of the studies have a control arm of non-delayed presentation patients to allow contemporaneous and direct comparison in the prevalence of pathology. The outcomes being measured have a low incidence. The established rate of clinically significant intra-cranial pathology following head injury is estimated at 5%, with only 1% of patients undergoing a neurosurgical procedure (Pandor et al., 2011). A protocol for a head injury study estimating the prevalence of significant intra-cranial injury in head injury patients taking warfarin calculated that a sample size of 3000 patients would be required to give an accurate estimate of such rare outcomes (Mason, 2011). All of the delayed presentation cohorts identified by the systematic review were far short of this number.

Barrow et al. 2012 is the only recent study and one that was conducted in the UK, where NICE guidelines are used. The 4-hour definition of delay is very short. This means that some patients defined as presenting in a delayed fashion are equivalent to patients who present within 4 hours to the ED, but who experience an unplanned delay to assessment and investigation by CT. The external validity of the population studied is also affected by it being a “young population with greater than 50% from the Indian sub-continent” (Barrow et al., 2012). The very high loss to follow up of patients who did not have CT scans and the low overall rate of pathology makes the study susceptible to attrition bias.

The study conducted by Hemphil et al. 1999 reports data from the USA and is relatively old. This means that it pre-dates current head injury guidelines for the use of CT for the investigation of head injury. It reports a relatively high rate of CT head scan for patients with mild head injury (52.1%), especially as it only included patients with a GCS of 15. This reflects practice in the USA at this time but means that the results of the study have less current applicability. No formal attempt to follow up patients who had not had scans was made and if they had not
re-attended at the same ED it is possible that intra-cranial pathology was under-reported in this study. This, coupled with the low rate of pathology, again makes the study highly susceptible to attrition and outlier bias.

The study presented by Borczuk et al (1997) is an abstract of a case series. Multiple attempts to contact the authors for more information were unsuccessful. This is understandable to an extent, as the abstract was published in 1995. The abstract includes no exclusion criteria or the total number of patients presenting after twenty-four hours of injury. The fact that the study was conducted in 1995 in the USA makes applying these results to current UK practice difficult. Based on the information available the internal and external validity of these data is questionable, especially in making judgments about current practice in the UK.

**Discussion**

This systematic review identified few studies of poor quality assessing whether delay in presentation affected the rate of intra-cranial pathology in patients presenting in a delayed fashion following a head injury. There is a large degree of clinical heterogeneity. The studies were conducted on different clinical populations with different clinical thresholds to mandate a CT scan. The nature of the studies identified precluded pooling of data to conduct a meta-analysis. A large systematic review found the median prevalence of intracranial injury in patients with minor/mild head injury to be 7.2% (Harnan et al., 2011). This rate is almost exclusively based on studies conducted in populations presenting within twenty-four hours. The rate of intra-cranial pathology reported in the studies identified by the systematic review was lower: 2.2% (Barrow et al., 2012); 3.1% (Hemphill et al., 1999); and 6.3% (Borczuk, 1997). However, this is an indirect comparison and two studies limited the population being studied to patients with a GCS of 15 or of 14/15. The 7.2% rate of pathology is derived from a population of patients with a definition of minor/mild head injury of GCS 13 or greater. As discussed before, excluding patients who present in a delayed fashion with
moderate/severe injuries potentially under-estimates the pathology rate in patients with minor head injury who present late, as these patients are likely to be patients with minor head injury who have clinically deteriorated.

It can also not be determined whether a potential reduction in intra-cranial pathology in those who have delayed presentation to the ED after head injury would translate to lower rates of neurosurgical intervention or death. Barrow et al (2012) reported similar rates of neurosurgical intervention to previous studies in patients presenting early after head injury (af Geijerstam et al., 2006, Fabbri et al., 2005), whereas Borczuk et al (1997) reported no patients requiring neurosurgical intervention in a pre-selected group who all underwent a CT head scan. The available evidence therefore suggests that delay in presentation may reduce the likelihood of intra-cranial pathology in patients with a mild head injury, but this evidence is weak.

**Weaknesses of the systematic review**

As detailed previously this systematic review was constrained by a lack of time and resources. This meant that only two electronic databases were searched. The AMSTAR measurement tool of systematic review methodological quality states that at least 2 electronic bases should be searched to meet minimum methodological requirements (Shea et al., 2009). This was achieved and searching databases that predominantly pertain to randomised control trials would have been inappropriate given the systematic review question. However, the “grey literature” was not searched in a systematic way and this means that unpublished studies may not have been identified. Hand searching of specific journals related to head trauma and emergency medicine research could have also been undertaken to identify non-indexed studies. This may have been particularly pertinent as the nature of the research area makes both the study design and topic difficult to categorise. The lack of studies identified prevented assessment of publication bias through funnel plotting.
In addition, although two independent reviewers undertook study selection and data extraction, they both had a similar clinical background as emergency physicians. This means that individual study selection biases are likely to be similar although the systematic review process is aimed at limiting this. The authors were not blinded to the publication details of studies under consideration during the study selection and data extraction components of the project as it was thought unfeasible. This may have introduced further bias, but the evidence of the utility of blinding appears to be limited. The systematic review did not formally assess sources of funding and conflicts of interest in included studies. This is slightly less relevant given the nature of the included studies and no studies seem to have been externally funded or be subject to conflict of interests. However, the AMSTAR checklist includes this as part of its methodological quality assessment (Shea et al., 2009).

Conclusion

The most important and valid conclusion of this systematic review is that there are only a few studies that are also of low quality that investigate the rate of intra-cranial pathology in patients who present in a delayed fashion. This is clinically relevant as the lack of research about this group makes their clinical risk assessment difficult, especially in those who present after twenty-four hours. Current NICE and other equivalent national guidelines like the NSW and CCHR are based upon research conducted on patients presenting within twenty-four hours of injury. The studies that have been identified suggest that patients who present in a delayed fashion may have a lower rate of intra-cranial pathology. They all are limited by methodological weakness and so therefore is the strength of any conclusions. However, the application of existing guidelines to mild/minor head injury patients presenting after twenty-four hours may risk over-investigating this group or fail to identify significant intra-cranial trauma. The review component of this project confirms in a methodical and reproducible
manner that there is insufficient evidence currently to aid and inform the clinical risk assessment of head injury patients who present in a delayed fashion.
3: Does delay in presentation affect clinician application of Emergency Department head injury guidelines? Clinical Vignette Based Survey

This chapter will present the findings from a clinical vignette survey. It tests whether clinicians’ application of NICE guidelines regarding the CT imaging of Emergency Department Head Injury Patients is affected by delay in presentation.

Introduction

As established previously, patients who present in a delayed fashion to the ED following a head injury, especially after twenty-four hours, comprise a group that existing research inadequately addresses. They may be a more benign sub-population at lower risk of deterioration (Choudhry et al., 2013) or a higher risk group due to the persistence of their symptoms (New South Wales Government Ministry of Health, 2012). Current UK guidelines (NICE) regarding the investigation and risk stratification of patients with head injury are based on the CCHR which have been derived and validated in a population presenting within twenty-four hours (NICE, 2014, Stiell et al., 2001). Existing guidelines may be less valid in patients who present in a delayed fashion and clinicians may be more likely to use their own judgment when deciding whether investigation of patient with a CT head is warranted.

Assessing Variation in Clinical Practice

A clinician survey provides a means to test whether clinicians apply existing guidelines to delayed presentation head injury patients. The use of vignettes in survey research has been well established since the early 1970s (Alexander and Becker, 1978, Evans et al.). It is particularly useful for assessing variation and performance in physician practice (Veloski et al., 2005). A clinical vignette is defined as “a brief written case history of a fictitious patient based on a realistic
clinical situation accompanied by one or more questions” (Veloski et al., 2005). Other validated means of detecting practice variation or evaluating clinical care involve either record abstraction or the use of standardised patients (Shah et al., 2010, Shah et al., 2007). All three methods have advantages and disadvantages in terms of their feasibility and methodological characteristics. The use of simulated or standardised patients is the gold standard for assessing clinical practice. However it is very resource intensive and can be susceptible to the Hawthorne effect, whereby performance is altered by observation (Shah et al., 2007, Veloski et al., 2005).

The time and resource limitations of this project preclude an examination of clinician decision making in delayed presentation head injury patients through the use of standardised or simulated patients. Clinical vignettes are recognised to be a cost effective and very efficient means of assessing clinician variation or quality, especially in relation to clinician performance against standards or guidelines (Veloski et al., 2005, Peabody et al., 2000). The main demonstrated disadvantage is that clinical vignettes overestimate clinician performance compared to that observed with simulated patients. (Shah et al., 2010, Peabody et al., 2000). This could be the result of the “sentinel effect”: a clinical vignette creates a situation where clinicians perceive they are being evaluated and therefore try to give the “correct” answer (Evans et al.).

Case note reviews have been observed to under-estimate clinician performance as not everything done by a clinician is accurately recorded (Shah et al., 2007). Also they are a more costly and time consuming method of evaluating clinician behaviour as compared to clinical vignettes (Veloski et al., 2005). The use of surveys to assess variation in practice between Emergency Departments in the UK is well established. The Royal College of Emergency Medicine has previously been willing to facilitate surveys of its members when pertinent subjects were being investigated (Dasan et al., 2014). It was therefore feasible and appropriate to attempt to evaluate whether there is variation in the application of current guidelines to patients with a delayed presentation head injury through a clinical
vignette based survey method targeted at Emergency Physicians, specifically members and fellows of the Royal College of Emergency Medicine.

**Aims**

The specific aims of this phase of the project were to explore, whether:

1. Whether a delay in presentation reduced clinician likelihood of requesting a CT head in line with existing guidelines.
2. Whether there was a consensus point at which the majority of clinicians felt minor head injury patients were free from the risk of deterioration and therefore stopped applying NICE guidance.
3. To assess whether there were clinical factors which altered clinicians’ risk assessment of delayed head injury patients.

**Methods**

**Vignette formulation**

The lack of a standardised method to formulate and test validity of clinical vignettes, despite their widespread use, has been acknowledged (Stacey et al., 2014). It is accepted that expert input with piloting and refinement of vignettes in an iterative process provides a common means for vignette development (Evans et al.). The scenarios used in vignettes should provide credible, real-world scenarios with sufficient information for clinicians to make relevant decisions. A small number of vignettes can capture a large amount of practice variation in a group of clinicians (Veloski et al., 2005). In the simplest form, altering or operationalising one factor in a vignette can be used to test variation in clinical practice. In this instance the clinical scenarios were drawn from the NICE head injury guidelines
(NICE, 2014). The selected independent variable was the time of presentation, and this was altered to see if it affected clinician decision making.

WT was consulted as head injury expert in establishing potential scenarios representing plausible clinical encounters with minor head injury patients that current NICE guidelines would recommend for investigation with CT head scan. Time of presentation was then operationalised in each scenario to test whether this affected the likelihood of clinicians utilising existing guidelines and requesting a CT head scan. Critics of vignette based methods argue that responses in such scenarios do not necessarily reflect real world behaviour (Evans et al.). As established earlier, vignettes tend to over-estimate adherence to guidelines (Shah et al., 2010). Nonetheless, they are accepted as a means to give an indication of clinician behaviour.

Two scenarios were initially formulated and piloted on a sample of middle grade and consultant emergency clinicians at Hull Royal Infirmary. This represents the group of clinicians who make decisions regarding which patients with head injury should receive CT head scans. Therefore, they were well placed to help formulate the vignettes. They were also a sample of the national population of this group that the project aimed to subsequently survey.

The scenarios were created and disseminated through the use of the Survey Monkey online survey tool. The survey requested feedback on how life-like the scenarios were, the ease of use of the format and how long the total survey took to complete. Sixteen out of twenty-five middle grade and consultant physicians responded. Feedback on how to make the vignettes clearer and which additional clinical factors were required to make a decision, were noted. A further consultation with WT and an Emergency Consultant based at Hull Royal Infirmary who had implemented NICE head injury guidelines locally, was arranged to create four final clinical vignettes. Feedback indicated that four was the maximum number of vignettes that could be completed within five minutes.
and five minutes was felt to be the optimum amount of time to maximise responses.

**The Vignettes**

Four vignettes were created. They represented paired scenarios where an additional clinical factor was added to the second of each pair. The first two scenarios were created as vignettes where the NICE guidelines mandated a CT scan due the circumstances of the injury and nature of patient. The patient was presented as attending the ED in an increasingly delayed fashion. Clinicians were asked if they would request a CT scan at an increasingly delayed time interval.

The first clinical vignette was of a sixty-seven year old patient presenting to the ED who had been knocked out due to a fall. The vignette presents further negative information regarding the narrative. Notably, that the hypothetical patient is asymptomatic when they present, the physical examination is unremarkable and the GCS is fifteen.

Current NICE guidelines would advise that for patients aged 65 and older who have experienced some loss of consciousness or amnesia, a CT head scan should be performed within eight hours of their injury (NICE, 2014). The CCHR derivation study identified a head injury in those over 65 when accompanied by loss of consciousness or amnesia, even when GCS was 15, two hours after the injury, as being high risk and at increased risk of neurosurgical pathology in a population of patients presenting within twenty-four hours (Stiell et al., 2001). Having presented a vignette of a patient for whom NICE guidelines would mandate a CT scan, respondents were asked if they would request a CT scan if the patient presented at each of: 8, 24, 48, 72, 96 hours and 1 week following the injury. The anticipated outcome was that the majority of clinician respondents would request a CT head scan at 8 hours, given the nature of the patient presenting. Time was then operationalised to test whether clinicians became less likely to request a CT head scan as the delay in presentation increased. The
underlying hypothesised clinical reasoning is that deterioration due to neurosurgical pathology will occur within a fixed acute time frame. After this hypothesised time period, neurosurgical pathology is ruled out.

The second vignette is designed to produce a scenario with superficial differences, but with the same salient information for clinical decision making with an additional factor of the patient taking warfarin. Warfarin’s anti-coagulant effect is known to increase the risk of primary and secondary intra-cranial haemorrhage following head injury (Docimo et al., 2014, NICE, 2014, Cohn et al., 2014). The current iteration of UK NICE guidelines recommends that for patients on warfarin who have sustained a head injury and have no other indication warranting a CT head scan, a scan should be performed within 8 hours. The vignette therefore presented respondents with a scenario in which there were two guideline-based indications for a CT scan. The times of presentation following the injury were given in an identical way as in the first scenario. The addition of warfarin was hypothesised to increase the likelihood of respondents requesting CT head scans at all times of presentation.

The third and fourth scenarios were paired in a similar manner to the first and second scenarios. The first and second scenarios describe an asymptomatic patient who was high risk at the point of injury, due to their demographics and nature of injury, presenting in an increasingly delayed manner. The third and fourth scenarios present an initially low risk patient presenting late due to the delayed onset of symptoms that then make them high risk. The third scenario is of a patient who has been punched in the head who attends hospital due to three episodes of vomiting in two hours. Respondents are asked whether they would request a CT head to investigate this patient if the onset of vomiting and accompanying time of presentation occurred at the same points in time as the original scenarios: 8, 24, 48, 72, 96 hours and 1 week following their injury. The fourth scenario is identical to the third, but the onset of vomiting is accompanied by a severe headache.
The CCHR derivation study identified more than one episode of vomiting following a head injury as a high risk factor that was independently predictive of neurosurgical pathology in patients presenting within twenty-four hours (Stiell et al., 2001). Current NICE guidance advises that for an adult who has sustained a head injury, a CT head scan should be completed within one hour of the identification of the risk factor of greater than one episode of vomiting. Therefore for both scenarios it was anticipated that the majority of clinicians would indicate that they would request a CT head at eight and twenty-four hours. After twenty-four hours it was thought that there would be increasing variation in responses with fewer clinicians requesting CT head scans as the onset of symptoms and presentation became increasingly delayed. This would reflect a model of clinical decision making in which deterioration following a head injury is thought to occur within a fixed time frame. It was postulated that, after this period, clinicians would no longer regard the vomiting as being related to the injury.

Headache was not found to be predictive of intra-cranial injury in the CCHR, but the New Orleans Study (Stiell et al., 2001, Haydel et al., 2000) identified it as being predictive of a traumatic finding on a CT head scan following a head injury. Additionally, discharge advice given to patients who have attended the ED following a head injury, is to return if they develop a severe or a persistent headache. One of the consultants involved in the development of the vignettes stated that it was his practice to request a CT scan in patients who presented in a delayed fashion or re-presented with a headache following a head injury. It was hypothesised that despite it not being part of NICE guidelines, the presence of a headache would increase the likelihood of respondents stating they would request a CT scan at each time period.
Vignette Dissemination

The initial model for survey dissemination and completion by respondents was through the College of Emergency Medicine (which became the Royal College of Emergency Medicine in March 2015). The Royal College of Emergency Medicine is “responsible for setting standards in training for Emergency Medicine and administering exams for the award of Fellowship and Membership to the College” in the UK (Royal College of Emergency Medicine Website 2015). The College therefore has contact information for all Members and Fellows of the College. Membership of the college is a prerequisite for becoming a registrar in emergency medicine and Fellowship is a condition for an ED becoming a consultant. This population therefore represents middle-grade and senior clinicians in Emergency Medicine. It is these clinicians who make decisions regarding which patients require investigation by a CT head scan.

The College is known to have previously facilitated contact with these groups through email in order to disseminate research surveys (Dasan et al., 2014). The Royal College of Emergency Medicine Research and Publications Committee have published guidelines regarding what criteria a proposed survey must meet for the College to disseminate it. A covering letter, copy of the survey and protocol for the dissemination of the clinical vignettes by the College was provided for the Research and Publications committee of the Royal College of Emergency Medicine. The committee advised that there were 2037 College Fellows and 2036 College Members in December 2014. After reviewing the protocol and the survey, the Royal College of Emergency Medicine agreed to disseminate the clinical vignettes.

However, the College rules regarding dissemination of such surveys had changed from the model previously noted (Dasan et al., 2014). The initial protocol planned for the college to send a covering email, with a hyperlink to an online Survey Monkey form of the clinical vignettes, to all Members and Fellows of the College.
Ideally, this would be repeated up to three times to maximise response rates. Multiple contact attempts have been demonstrated to optimise survey response rates (VanGeest et al., 2007, Grava-Gubins and Scott, 2008). The Research and Publications committee advised the research team that surveys were no longer emailed directly to Members and Fellows due the very high number of surveys in which the College participated. Research survey hyperlinks were now distributed to members and fellows as part of the monthly College online newsletter that was sent by email to all Members and Fellows. Surveys were also advertised on the Royal College of Emergency Medicine website. The Royal College approved these routes of survey dissemination for delayed-presentation head injury clinical vignettes.

This change in rules substantially reduced the degree of exposure for the vignette survey. The associated response rate was therefore also expected to be significantly reduced. Physicians are a group that have been observed to respond poorly to surveys (VanGeest et al., 2007). The Canadian National Physician survey is a large training-needs assessment survey of physicians that occurs every three years. It is conducted in collaboration with the national bodies responsible for medical training in Canada. Despite being well publicised and multiple methods being employed to maximise responses, survey response rates in 2007 were 31.6% (Grava-Gubins and Scott, 2008).

Given the high workload of emergency physicians and the academic nature of the survey, maximizing the number of survey responses was anticipated to be problematic. Therefore, in addition to dissemination through the College, other methods were explored. Previous postal surveys had assessed departmental practice by contacting the clinical leads at each individual Emergency Department (Smith and Mason, 2012, Goodacre et al., 2010). The nature of this survey differed in that the aim was to maximise responses from individual decision-making clinicians as opposed to appraising practice at a departmental level. However, contact with clinical leads was noted as a method of disseminating research surveys. The research team had access to the list of active type one
Emergency Departments in the UK as previously surveyed by Smith and Mason in 2012. This had been compiled in 2010 from a list of Emergency Departments in the UK which was available from the College of Emergency Medicine and from the NHS Choices website. This list was cross-checked against individual NHS Trust websites and the information available at the NHS choices website. Checks were also made with individual hospitals. This final list therefore comprised an up-to-date record of every Emergency Department in the UK. This amounted to 186 hospitals in England and Wales, Ten hospitals in Northern Ireland and Seventeen Hospitals in Scotland.

Attempts were then made to contact the Emergency Medicine clinical lead at each of these hospitals. This was done by phoning each hospital and liaising with the Emergency Department secretaries. The contact details of the clinical lead or their personal assistants were requested. A covering email which included a web link to the online survey was then sent directly, or forwarded by their secretary, to the relevant clinical lead. The covering email requested that: the web link to the online survey be circulated to consultants and middle-grade doctors at each department; and an email be sent back to the research team when this was done.

**Research Ethics**

The scope of the survey was a fully anonymised clinician survey involving hypothetical clinical vignettes of scenarios that represented routine practice for emergency physicians. The Health Research Authority decision tool was consulted. As the survey did not involve NHS service users, approval from a NHS research ethics committee was not required. The College of Emergency Medicine guidelines regarding dissemination of surveys stated that ethical review prior to dissemination may be appropriate when information regarding individual patients, non-routine hospital data, or potentially controversial or sensitive professional opinions are requested. It was felt that the clinical vignette based survey did not fall into any of these categories. The Royal College of Emergency
Medicine were satisfied that a research ethics committee review was not necessary prior to the dissemination of the survey. Finally, the chair of the Hull York Medical School Ethics committee was contacted and he was satisfied that as the survey simply asked clinicians how they would manage four theoretical scenarios, formal ethics committee review was not required.

**Results**

The survey was released as part of the on-line December 2014 Royal College of Emergency Medicine newsletter. The clinical leads of each Emergency Department in the UK were contacted in January to March 2015. The survey was closed on the 21/4/2015. As there were 2037 Fellows of the College and 2036 Members, the number of middle grade and consultant Emergency physicians in the UK was estimated to be approximately 4,073.

The list of Emergency Departments in the UK included 245 hospitals. Sixteen of these were found to be minor injury units or no longer had Emergency Departments. Fourteen were joint Trusts and two were dedicated paediatric Emergency Departments. This left 213 relevant Emergency Departments. As the formative survey had been piloted at Hull Royal Infirmary, that hospital was excluded, leaving 212 Emergency Departments. Of these 207 Emergency Departments were contactable. The clinical leads at the remaining five departments were not contactable, despite multiple attempts by the research team. Two contacted departments declined to participate. Hospitals in Scotland were sent a different web link to allow comparison between Scotland and the rest of the UK, as Scotland uses SIGN head injury guidelines, that differ from NICE. The results are presented in tables 2 and 3. An email to confirm receipt and distribution of the survey was received by members of the research team for seventy-four hospitals. Confirmation of receipt of the survey was made by telephone for the remaining hospitals.
Response Rate

The overall response rate was 449 from an estimated population of 4073, this equates to a 11% response rate. There was an attrition rate of 16.7% with only 374 respondents to the final question. Table 2 presents the proportion of clinicians who would request CT scan for each question, at each given time, in total and stratified by grade. Table 3 shows the proportion of clinicians who would request a CT scan for each question, at each time interval, in total and stratified by whether the response was from England, Wales and Northern Ireland, or Scotland. Responses generated via the web link disseminated through the College newsletter are not included in the stratification in Table 3, as the web-link was sent to members and fellows, irrespective of their locality.

The 95% confidence interval for each percentage is given in brackets. The confidence interval is calculated by each proportion +/- 1.96*sqrt(p(1-p)/n) providing np and n(1-p) is greater than 5. Where this is not the case no confidence interval is given.
Table 2: Proportion of respondents that would request a CT head scan stratified by grade of (95% C.I. given in brackets)

<table>
<thead>
<tr>
<th>Question</th>
<th>Would request a Scan at 8 hours</th>
<th>Would request a Scan at 24 hours</th>
<th>Would request a Scan at 48 hours</th>
<th>Would request a Scan at 72 hours</th>
<th>Would request a Scan at 96 hours</th>
<th>Would request a Scan at 1 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 N=414</td>
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</tr>
<tr>
<td>Consultants</td>
<td>42.9% (36.7-49.1)</td>
<td>22.7% (17.5-27.9)</td>
<td>13.0% (8.8-17.2)</td>
<td>9.7% (6-13.4)</td>
<td>8.1% (4.7-11.5)</td>
<td>7.3% (4.1-10.5)</td>
</tr>
<tr>
<td>Middle Grades</td>
<td>45.5% (37.9-53.1)</td>
<td>20.4% (14.3-26.5)</td>
<td>10.2% (5.6-14.8)</td>
<td>7.2% (3.3-11.1)</td>
<td>5.4% (2.0-8.8)</td>
<td>4.8% (1.6-8.0)</td>
</tr>
<tr>
<td>2 N=403</td>
<td>94.8% (92.6-97)</td>
<td>82.1% (78.4-85.8)</td>
<td>61.5% (56.7-66.3)</td>
<td>47.6% (42.7-52.5)</td>
<td>41.9% (37.1-46.7)</td>
<td>39.5% (34.7-44.3)</td>
</tr>
<tr>
<td>Consultants</td>
<td>94.6% (92.3-96.9)</td>
<td>81.7% (76.8-86.6)</td>
<td>63.3% (57.2-69.4)</td>
<td>52.1% (45.8-58.4)</td>
<td>45.8% (39.5-52.1)</td>
<td>43.8% (37.5-50.1)</td>
</tr>
<tr>
<td>Middle Grades</td>
<td>95.1% (91.8-98.4)</td>
<td>82.8% (77.0-88.6)</td>
<td>58.9% (51.3-66.5)</td>
<td>41.1% (33.5-48.7)</td>
<td>36.2% (28.8-43.6)</td>
<td>33.1% (25.9-40.3)</td>
</tr>
<tr>
<td>3 N=389</td>
<td>85.3% (81.8-88.8)</td>
<td>76.9% (72.7-81.1)</td>
<td>54.5% (49.6-59.4)</td>
<td>37.8% (33-42.6)</td>
<td>28.3% (23.8-32.8)</td>
<td>23.9% (19.7-28.1)</td>
</tr>
<tr>
<td>Consultants</td>
<td>84.3% (79.6-89.0)</td>
<td>78.2% (72.9-83.5)</td>
<td>60.7% (54.4-67.0)</td>
<td>46.3% (39.8-52.8)</td>
<td>35.8% (29.6-42.0)</td>
<td>29.7% (23.8-35.6)</td>
</tr>
<tr>
<td>Middle Grades</td>
<td>86.9% (81.7-92.1)</td>
<td>75.0% (68.3-81.7)</td>
<td>45.6% (37.9-53.3)</td>
<td>25.6% (18.8-32.4)</td>
<td>17.5% (11.6-23.4)</td>
<td>15.6% (10.0-21.2)</td>
</tr>
<tr>
<td>4 N=381</td>
<td>98.4% (97.1-99.7)</td>
<td>95.0% (92.8-97.2)</td>
<td>87.1% (83.7-90.5)</td>
<td>78.2% (74.1-82.3)</td>
<td>70.3% (65.7-74.9)</td>
<td>66.7% (62.0-71.4)</td>
</tr>
<tr>
<td>Consultants</td>
<td>98.7% (94.0-98.8)</td>
<td>96.4% (94.0-98.8)</td>
<td>91.1% (87.4-94.8)</td>
<td>84.9% (80.2-89.6)</td>
<td>79.6% (74.3-84.9)</td>
<td>76.0% (70.4-81.6)</td>
</tr>
<tr>
<td>Middle Grades</td>
<td>98.1% (88.9-96.9)</td>
<td>92.9% (88.9-96.9)</td>
<td>81.4% (75.4-87.4)</td>
<td>68.6% (61.3-75.9)</td>
<td>57.1% (49.3-64.9)</td>
<td>53.2% (45.4-61)</td>
</tr>
</tbody>
</table>
Table 3: Proportion of respondents that would request a CT head scan stratified by location (95% C.I. given in brackets)

<table>
<thead>
<tr>
<th>Question</th>
<th>Would request a Scan at 8 hours</th>
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<td>1</td>
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</tr>
<tr>
<td>N=414</td>
<td>44.0% (39.2-48.8)</td>
<td>21.7% (16.6-26.8)</td>
<td>11.8% (8.7-14.9)</td>
<td>8.7% (6.0-11.4)</td>
<td>7.0% (4.5-9.5)</td>
<td>6.3% (4.0-8.6)</td>
</tr>
<tr>
<td>Eng/Wales/NI 335</td>
<td>46.0% (40.7-51.3)</td>
<td>22.0% (17.6-26.4)</td>
<td>11.9% (8.0-15.8)</td>
<td>9.3% (6.2-12.4)</td>
<td>7.5% (5.0-10.0)</td>
<td>6.3% (3.7-8.9)</td>
</tr>
<tr>
<td>Scotland 42</td>
<td>23.8% (10.9-36.7)</td>
<td>9.5%</td>
<td>4.8%</td>
<td>2.4%</td>
<td>0</td>
<td>2.4%</td>
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<td>2</td>
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<td></td>
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<td>61.5% (56.7-66.3)</td>
<td>47.6% (42.7-52.5)</td>
<td>41.9% (37.1-46.7)</td>
<td>39.5% (34.7-44.3)</td>
</tr>
<tr>
<td>Eng/Wales/NI 326</td>
<td>94.8% (92.4-97.2)</td>
<td>82.8% (78.7-86.9)</td>
<td>61.7% (56.4-67.0)</td>
<td>47.2% (41.8-52.6)</td>
<td>41.4% (36.1-46.7)</td>
<td>39.6% (34.3-44.9)</td>
</tr>
<tr>
<td>Scotland 41</td>
<td>90.2% (54.1-82.5)</td>
<td>68.3% (54.1-82.5)</td>
<td>46.3% (31.5-69.6)</td>
<td>31.7% (17.5-45.9)</td>
<td>29.3% (15.4-43.2)</td>
<td>26.8% (13.2-40.4)</td>
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<td>3</td>
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</tr>
<tr>
<td>N=389</td>
<td>85.3% (81.8-88.8)</td>
<td>76.9% (72.7-81.1)</td>
<td>54.5% (49.6-59.4)</td>
<td>37.8% (33.0-42.6)</td>
<td>28.3% (23.8-32.8)</td>
<td>23.9% (19.7-28.1)</td>
</tr>
<tr>
<td>Eng/Wales/NI 313</td>
<td>85.6% (81.7-89.5)</td>
<td>77.3% (72.7-81.9)</td>
<td>55.6% (50.1-60.1)</td>
<td>38.3% (32.9-43.7)</td>
<td>29.1% (24.1-34.1)</td>
<td>24.6% (19.8-29.4)</td>
</tr>
<tr>
<td>Scotland 40</td>
<td>80.0% (67.6-92.4)</td>
<td>72.5% (58.7-86.3)</td>
<td>47.5% (32.6-63)</td>
<td>35.0% (20.2-49.8)</td>
<td>27.5% (13.7-41.3)</td>
<td>22.5% (9.6-35.4)</td>
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<tr>
<td>N=381</td>
<td>98.4% (97.1-99.7)</td>
<td>95.0% (92.8-97.2)</td>
<td>87.1% (83.7-90.5)</td>
<td>78.2% (74.1-82.3)</td>
<td>70.3% (65.7-74.9)</td>
<td>66.7% (62-71.4)</td>
</tr>
<tr>
<td>Eng/Wales/NI 308</td>
<td>98.1% (96.6-99.6)</td>
<td>94.8% (92.3-97.3)</td>
<td>87.0% (83.2-90.8)</td>
<td>77.9% (73.3-82.5)</td>
<td>70.5% (65.4-75.6)</td>
<td>66.9% (51.6-72.2)</td>
</tr>
<tr>
<td>Scotland 38</td>
<td>100%</td>
<td>97.4%</td>
<td>86.8% (76.2-97.4)</td>
<td>84.2% (72.6-95.8)</td>
<td>76.3% (62.8-89.8)</td>
<td>71.1% (56.7-85.5)</td>
</tr>
</tbody>
</table>
Clinical Vignette 1

Figure 2: Scenario presented in clinical vignette 1

Question 1

A 67 year old woman trips over a chair and bangs her head. She was knocked out but now feels fine. She attends the emergency department to be checked over. Her GCS is 15, observations and examination are normal. There are no neurological deficits or signs of a skull fracture.

She is on no medications, has not fitted and has no amnesia.

Would you request a CT scan of her head if she attended:

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 hours following the injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hours following the injury?</td>
<td></td>
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<tr>
<td>48 hours following the injury?</td>
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</tr>
<tr>
<td>72 hours following the injury?</td>
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<tr>
<td>96 hours following the injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 week following the injury?</td>
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</tbody>
</table>

The clinical vignette in question 1 presents a sixty-seven year old who has fallen and been knocked out. Current NICE guidelines would recommend a CT scan of such a patient and the evidence from original CCHR study would indicate that this was a high-risk patient with potential neurosurgical pathology (Stiell et al., 2001). The responses to question are summarized in figures 3 and 4 below. Significantly, even with a delay of presentation of eight hours, the majority of clinicians who responded indicated that they would not request a CT scan to investigate such a patient. Overall, only forty-four per cent of clinicians indicated they would request a CT scan for such a patient if they presented asymptomatically eight hours following their injury.
Figure 3: Vignette 1 proportion of clinicians that would request a CT head scan stratified by grade

![Bar chart showing the proportion of clinicians who would request a CT head scan at different time points for all grades, consultants, and middle grades.](image)

Figure 4: Vignette 1 proportion of clinicians that would request a CT head scan stratified by location of hospital

![Bar chart showing the proportion of clinicians who would request a CT head scan at different time points for England/Wales/NI and Scotland.](image)

This is most pronounced in those responding from Scottish hospitals where respondents were around half as likely to request a CT scan when compared to clinicians in other parts of the UK. Further delay in presentation reduced the likelihood of clinicians requesting a CT scan. At a delay in presentation of seventy-two hours, less than 10% of clinicians who responded stated that they would request a CT scan for such a patient. The implication is that clinicians regard a delay in presentation, in the clinical vignette presented in question one, as
reducing the risk of traumatic intra-cranial pathology. Indeed, despite the recommendations of NICE guidance for a scenario such as that described above involving the seventy-five year old, the majority of clinicians who responded regard eight hours as sufficient time to negate the need for a CT scan to rule out serious traumatic pathology,

Clinical vignette 2

Figure 5: Scenario presented in vignette 2

Question 2

A 67 year old man trips over and bangs his head. He is also knocked out but now feels fine. His examination and observations are normal. His GCS is 15 and there is no neurological deficit. He has had no seizures or vomiting.

He has no amnesia but is on warfarin for AF.

Would you request a CT scan of his head if he attended:

<table>
<thead>
<tr>
<th>Time following the injury</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 hours</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>24 hours</td>
<td>☐</td>
<td>☐</td>
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<td>48 hours</td>
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<td>☐</td>
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<tr>
<td>72 hours</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>96 hours</td>
<td>☐</td>
<td>☐</td>
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<tr>
<td>1 week</td>
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Question 2 presented an identical clinical situation to the first question with the addition of the hypothetical patient taking warfarin. This significantly increased the likelihood of clinicians requesting a CT scan to investigate the presented patient at all time intervals when compared to question 1. The results are
summarised in figures 6 and 7 below. The vast majority of clinicians (82.1%) would request a CT scan to investigate such a patient up to twenty-four hours of injury. There was divergence in the sample at 72 hours delay with approximately half of clinicians indicating they would still request a CT scan for such a patient. Interestingly, almost 40% of clinicians stated that even following a delay in presentation of a week they would request a CT head scan. There is clear divergence in clinical opinion for the management of such a patient. By 72 hours about half of clinicians regard the presence of a NICE indications for a CT head scan as being less predictive of significant intra-cranial injuries. However, warfarin was regarded as increasing the risk of intra-cranial pathology and was perceived as increasing the time following the initial injury at which such pathology can manifest clinically.

Figure 6: Vignette 2 proportion of clinicians that would request a CT head scan stratified by grade
Clinical vignette 3

Figure 8: Scenario presented in vignette 3

Question 3

A 28 year old man presents to the Emergency Department to be checked over after being punched in the head during a night out.

He has a black eye but no signs of a skull fracture.

His observations and examination are normal, GCS is 15 and there is no neurological deficit.

He remembers what happened and was not knocked out.

He has not fitted.

He is usually fit and well and is on no medications.

He attends hospital because he has unusually vomited three times in 2 hours.

Would you request a CT scan of his head if the vomiting developed:

<table>
<thead>
<tr>
<th>Time Following Injury</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 hours</td>
<td></td>
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<tr>
<td>24 hours</td>
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<td>72 hours</td>
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<tr>
<td>96 hours</td>
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<tr>
<td>1 week</td>
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</table>
Question 3 presents the scenario of a patient who has developed vomiting in a delayed fashion following a head injury. Greater than one episode of vomiting was demonstrated to be a high risk factor which correlated with an increased risk of neurosurgical pathology in the CCHR study (Stiell et al., 2001) and is a NICE indication for an immediate CT head. The responses to this question are summarised in figures 9 and 10 below. In accordance with NICE guidance the majority of clinicians would request a CT head scan of the presented patient until 48 hours of symptoms developing.

**Figure 9: Vignette 3 proportion of clinicians that would request a CT head scan stratified by grade**
At this point there is variation in practice with around half of clinicians indicating that they would still request a CT head for such a postulated patient. At 72 hours the majority of respondents stated they would not request a CT head, implying that at this time since injury the majority of clinicians regard the onset of vomiting not to be predictive of serious traumatic intracranial pathology. However, at a week after injury, approximately 20% clinicians still would request a CT head scan. There is evidence of clinical uncertainty regarding the significance of post head injury vomiting after twenty-four hours.
Clinical vignette 4

Figure 11: Scenario presented in vignette 4

Question 4

The same 28 year old man attends the emergency department as in the previous question.

However he attends hospital because he has vomited three times in 2 hours and has developed a severe headache.

Would you request a CT scan of his head if the vomiting and headache developed:

<table>
<thead>
<tr>
<th>Time after injury</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 hours</td>
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<tr>
<td>24 hours</td>
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<tr>
<td>48 hours</td>
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<td>72 hours</td>
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<tr>
<td>96 hours</td>
<td></td>
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<tr>
<td>1 week</td>
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The clinical vignette presented in question 4 is the same as question 3, but the hypothetical patient has a delayed onset headache in addition to vomiting. The responses to this vignette are summarised in figures 12 and 13 below. Although not an indication for a CT head scan present in the NICE guidelines, the presence of a headache increased the likelihood of respondents requesting a CT head scan at all time intervals presented. The increase is particularly pronounced at the 72 hour interval and the delay in presentation time intervals after this. The presence of a headache more than doubles the number of respondents who would request a CT head scan at 72, 96 hours and at one week in scenario 4 compared to scenario 3. The relative risk of requesting a CT head scan at 72 hours in scenario 4 compared to scenario 3 is 2.1, at 96 hours it is 2.5 and at 1 week the relative risk is 2.8. The more delayed the presentation, the greater the affect of the presence of a headache in altering clinician behaviour. Even at a week following the injury 66.7% of respondents indicated that they would request a CT head to investigate the patient presented in the 4th clinical vignette. Irrespective of time of
presentation, the majority of clinicians regarded the presence of a headache and vomiting to mandate a CT head to exclude the presence of serious intra-cranial pathology following a head injury.

Figure 12: Vignette 4 proportion of clinicians that would request a CT head scan stratified by grade

Figure 13: Vignette 4 proportion of clinicians that would request a CT head scan stratified by location of hospital
Question 5: Guidelines

The final question in the survey asked respondents if the Emergency Department in which they worked had any guidelines specific to patients presenting after twenty-four hours and if their so, to provide details. This reflects that current national UK guidelines (NICE and SIGN) are based on studies of patients presenting within twenty-four hours of their injury and make no recommendations regarding the management of patients presenting in a delayed fashion. Only 13.1% of respondents (49 clinicians) stated that the Emergency Department at which they worked had such a guideline. Forty of the 49 clinicians specified what these guidelines were. Significantly, 60% of respondents cited NICE or SIGN guidelines as those used by the departments to manage patients with head injuries presenting after twenty-four hours of injury. Only 10 respondents outlined the specific guidelines of their departments for patients presenting after twenty-four hours. The NSW guidelines were cited by one such respondent, with the other respondents indicating they would request a CT head scan for patients presenting in a delayed fashion if they were taking anti-coagulants or had persistent symptoms. Six respondents stated that patients who presented after twenty-four hours following a head injury received a senior clinician review. The remaining respondents either stated that their department currently does not have guidelines for patients presenting after twenty-four hours or outlined general management principles of patients with head injury that were not specific to patients presenting after twenty-four hours.
Discussion

Key findings

The responses to the clinical vignettes provides evidence that delay in presentation reduces the likelihood that clinicians will follow NICE guidelines indicating that patients should be investigated with a CT head scan following a head injury. There is significant variation in the responses to the scenarios indicating a lack of clinical consensus regarding the management of delayed presentation head injury patients. In two of the scenarios a position of clinical equipoise was identified at a delay in presentation of approximately 48 hours. Factors not present in the NICE guidelines were found to affect how clinicians stated they would mange this group. Clinicians were also generally unaware of any guidelines or resources that could be used to aid clinical decision making about the CT head imaging of delayed presentation head injury patients.

Limitations of the study

If the number of Members and Fellows of the Royal College of Emergency Medicine is a true estimate of how many middle grade and consultant Emergency Physicians there are in the UK, only an 11% response rate was achieved. In addition there was an attrition rate of 15% from the first question to the end of the final clinical vignette. This makes this study susceptible to both non-response and attrition bias. Non-response bias occurs where there is a systematic difference between respondents to a survey and non-respondents, making the results of a survey biased (Barclay et al., 2002). Due to the limitations in how the survey was disseminated and the large scale of the survey population, only an 11% response rate was achieved. Notably, survey reminders could not be sent as the survey was disseminated through intermediary parties in the form of the College of Emergency Medicine and emergency department clinical leads.
How externally valid the responses of the survey are to the behaviour of all Emergency Clinicians in the UK depends on how representative and generalisable the sample of respondents is. This is difficult to assess. However, responses to the survey indicated that 60.1% of respondents were consultants, and the remaining respondents were middle and training grade doctors. In the Emergency Department in Hull Royal Infirmary when the survey was initially piloted there were 25 middle grade and consultant physicians in Emergency Medicine. Of these, forty-eight per cent of the doctors were middle grades. In addition to this there are similar numbers of College Members as there are Fellows; 2036 and 2037, respectively.

This indicates that survey respondents disproportionately comprised consultant emergency physicians. This may reflect a systematic tendency for more consultant physicians to be sampled as the survey was sent to clinical leads at individual emergency departments in order to be distributed to their colleagues. Middle grade respondents were less likely to indicate that they would request a CT scan 72, 96 hours and 1 week than consultant physicians in vignettes 2, 3 and 4. This difference was statistically significant in vignettes 3 and 4. This indicates that the overall response to the survey may overestimate the tendency of clinicians to request CT head scans as a delay in presentation following a head injury, increases. It is not possible to assess whether other systematic differences between non-responders and respondents exist. It is feasible that clinicians with a specific interest or clinical perspective regarding the management of head injuries may have been more likely to respond and respond in a different way, to a “typical” Emergency Physician.

The internal validity of this clinical vignette based survey is dependent upon how well the vignettes simulate plausible clinical scenarios and how truthfully clinicians responded. A common criticism of the vignettes from clinicians who participated was that they felt that it was unrealistic that a patient would present three days to a week following a head injury if they were asymptomatic. This was a scenario presented in the first and second clinical vignettes. As discussed in
chapter 4, analysis of the audit head injury data collected at Hull Royal Infirmary indicates that approximately 30% of patients who present in a delayed fashion are in fact asymptomatic and these patients can present after a week following their injury. However, perception of this scenario being unrealistic may have affected clinician responses.

The psychometric characteristics of clinical vignettes in general and in this particular survey are not well validated. Clinician responses to clinical vignettes tend to overestimate their performance and application of guidelines (Shah et al., 2010, Veloski et al., 2005). Therefore responses, especially at eight, and twenty-four hour intervals, where NICE guidelines would advise requesting a CT head to investigate a patient, may overestimate the likelihood of clinicians requesting CT head scans for the postulated patients. The survey had a fixed order and it was designed in a manner that prevented respondents returning to previous questions in order to change their answers. The survey’s structure was intended to prevent information presented in later questions influencing responses to earlier questions. Specifically, it was felt that the final question regarding knowledge of head injury guidelines could act retrospectively to influence clinician response. However, creating a fixed order with the deliberate pairing of scenarios may have influenced how clinicians responded. Information given in previous scenarios may have influenced clinicians’ responses and the step-wise addition of a factor like warfarin or a headache may have given these factors over-emphasis or implied significance resulting in an overestimation of how clinicians would have responded. This may have resulted in clinicians over-estimating how likely they would be to request a CT scan in scenarios 2 and 4. Randomising or counter-balancing the order of the scenarios would have been means in which carry-over and order effects could have been controlled for.
Implications of findings

The results of the clinical vignette survey suggest strongly that clinicians regard delay in presentation as being protective in patients with minor head injury. The number of respondents that indicated they would request a CT scan to investigate the hypothetical patients presented in each vignette decreased as the time interval from the time of injury and presentation increased. This is despite there being a clear NICE guideline indication for a CT scan in each vignette. This indicates that clinicians regard NICE guidelines to be less relevant in delayed presentation head injury patients. There was also significant clinical divergence of opinion demonstrated in all the vignettes at almost all the time intervals. With the exception of the first vignette, even at the extreme of presentation of a week, a clinical consensus of over 80% of respondents was not reached. This indicates a lack of a shared clinical approach to the risk assessment of delayed presentation minor head injury patients.

Significantly, the majority of clinicians indicated that even at eight hours they would not request a CT head scan to investigate a sixty-seven year-old patient who had been knocked out by a fall as presented in the first clinical vignette. This is despite good evidence that such a patient presenting within twenty-four hours (Stiell et al., 2001) is at risk of neurosurgical pathology, and despite the current NICE guidance. This fits with a clinical model of traumatic pathology in patients with minor head injury in which such pathology will manifest through deterioration or new symptoms within a fixed time period. After this time period has elapsed the patient is no longer at risk of deterioration from traumatic pathology and therefore application of NICE guidance and investigation through a CT head scan is no longer warranted.

There is some evidence to support this model with a cohort of patients with minor head injuries and intra-cranial haemorrhage having been found to deteriorate within twenty-four hours (Choudhry et al., 2013). This evidence is not conclusive,
but the results of the survey strongly suggest that Emergency Physicians ascribe to this model with only 21.7% of clinicians indicating that they would request a CT scan for the NICE “positive” patient at twenty-four hours as presented in the first clinical vignette. The addition of warfarin in the second clinical vignette resulted in an increase in the number clinicians indicating they would request a CT head scan across all time intervals. Notably nearly 50% of clinicians would still request a CT scan at 72 hours and nearly 40% of clinicians would request a CT scan at a week. This change in behaviour may reflect a clinical awareness of an increased baseline risk of traumatic intra-cranial pathology in anti-coagulated patients or recognition of the higher risk of secondary intra-cranial haemorrhage (Docimo et al., 2014). Either way, anti-coagulated patients are at a higher perceived risk of traumatic intra-cranial pathology and the time in which such pathology can manifest is also perceived as being longer.

The 3rd clinical vignette indicates that the majority of clinicians view the onset of vomiting as predictive of traumatic intra-cranial pathology in patients with a minor head injury until the seventy-two hour time interval. At this time interval, and at the subsequent time intervals, the majority of respondents stated they would not request a CT head scan. This implies they no longer regard the onset of vomiting to be predictive of intra-cranial pathology. This may be because by seventy-two hours clinicians regard the postulated patient to be safe from deterioration from a head injury and the vomiting to be due to a different pathology. The addition of a headache to the vignette makes clinicians more likely to request a CT scan across all the time intervals and the effect is particularly large as the delay in presentation is more extreme. This is despite a headache not being part of NICE guidelines regarding the management of patients with head injury. This probably reflects a clinical view, as expressed by a consultant involved in the formulation of the vignettes, that a delayed onset of a headache is indicative of a delayed or slowly accumulating intra-cranial haemorrhage. However, there is currently no evidence to support such a seemingly widely held view.
Conclusion

The responses to the clinical vignettes indicate that clinicians are less likely to apply NICE guidelines to patients who present in a delayed manner. This implies that clinicians regard factors included in the NICE guidelines to be less relevant in the risk assessment of head injury patients presenting in a delayed manner. At what point clinicians stop applying NICE guidelines to patients presenting in a delayed fashion, is dependent on the specific NICE indication for a CT head scan. There is evidence of clinicians subscribing to a model in which deterioration in minor head injury occurs within a fixed time period. The length of this time period is flexible and dependent upon clinical circumstances. The anti-coagulation of patients or the presence of a headache were viewed as increasing the risk of intra-cranial pathology in patients with the longest delays in presentation. The strength of these conclusions are limited by the internal validity of the clinical vignette method and the external validity of the ED clinician sample.
Chapter 4 Analysis of audit data:

This chapter uses routinely collected audit data related to six months of head injury attendances to the ED at Hull Royal Infirmary to characterise the size and nature of the population of head injury patients that present after twenty-four hours of injury. These data are also used to compare the prevalence of intra-cranial injury in patients presenting after twenty-four hours to a non-delayed comparator sample group. The use and sensitivity of existing NICE head injury guidelines are also assessed in those presenting after twenty-four hours of injury.

Introduction

This project has so far outlined the clinical background to the management of head injuries in the UK ED. NICE guidelines are used to triage the ninety-five per cent of patients with minor/mild head injuries into patients that can be discharged on the basis of the history and examination and those who require a CT head scan to exclude serious intra-cranial pathology (NICE, 2014). These guidelines are based on the CCHR, which was derived and validated in populations presenting within twenty-four hours of their injury (Stiell et al., 2001, Harnan et al., 2011). The systematic review component of the project has demonstrated that there are few studies addressing patients who present in a delayed manner following injury. Furthermore, there were no studies, apart from a research abstract, that addressed patients presenting after twenty-four hours of injury. The clinical vignette based survey of emergency physicians shows that clinicians may regard current guidelines to be less relevant to patients who present after twenty-four hours.

This final phase of the project uses six months of routine head injury data collected for the purposes of audit at Hull Royal Infirmary. These data included six months of emergency department notes for attendances to the Hull Royal Infirmary following a head injury as identified by retrospective hand searches by a
dedicated departmental research nurse for the period 14/11/11 to 14/5/12. These could be matched to the electronic radiology reporting system. For the same time period the department had an electronic record of all CT head scans requested by the Hull Royal Infirmary Emergency Department. These requests could be matched to the electronically stored Emergency Department notes for these patients and the results of the corresponding CT head scans. These data were used to accomplish the aims and objectives outlined below.

Aims and Objectives

Given the uncertainty regarding the size, nature and risk profile of delayed presentation head injury patients, the overall aim of this part of the project was to: assess the size of the population of head injury patients presenting after twenty-four hours and whether the NICE guidelines were as relevant to the clinical risk assessment of this group.

The specific objectives were:

i) **Assess what proportion of CT head scans for head trauma, and head injury attendances, are for adult patients presenting after 24 hours of injury.**

Most studies in head injury have been aimed at better assessing risk in patients with minor head injury. These studies have been almost exclusively conducted on patients presenting within twenty-four hours (Harnan et al., 2011). Very little data is available to estimate how large, and therefore clinically important, the population of patients is that present after twenty-four hours. One third of approximately 500 patients who presented after four hours, following a head injury, were found to have presented after twenty-four hours in one recent UK based study (Barrow et al., 2012). In an older comparable American study only 6.7% patients with head injury were found to present after twelve hours (Hemphill et al., 1999). If patients presenting after twenty-four hours did not represent a
group large enough to be clinically significant population, then further research in this area is not warranted.

II) **Compare the prevalence of significant intra-cranial injuries identified by CT imaging in adult head injury patients presenting within, and after, 24 hours of injury.**

There is evidence that clinical deterioration from significant intra-cranial pathology occurs within a fixed time frame and this time frame is usually within twenty-four hours (Choudhry et al., 2013, Reynolds et al., 2003, Alahmadi et al., 2010). This informs current head-injury discharge advice given to patients: that a responsible adult should supervise them for twenty-four hours following their injury. If significant intra-cranial pathology mostly manifests within twenty-four hours then the proportion of patients with intra-cranial injury identified by CT scan should be significantly less in those presenting after twenty-four hours.

III) **Compare the adherence to, and the sensitivity of, the NICE head injury guidelines in adult head injury patients that have undergone CT head imaging presenting within, and after twenty-four, hours of injury.**

The NICE guidelines were specifically aimed at the management of patients with head injury presenting within twenty-four hours of injury (personal correspondence with Dr Christopher Rowland Hill Consultant Neuroradiologist, Guideline development group 2003, 2007). It is based on the CCHR, which was derived from a population presenting within twenty-four hours. Furthermore, the CCHR and NICE guidelines have only been validated in populations presenting within twenty-four hours (Fabbri et al., 2005, NICE, 2014, Smits et al., 2007, Harnan et al., 2011, Smits et al., 2005, Stiell et al., 2001). As outlined previously patients presenting after twenty-four hours may represent a distinct sub-population. Clinicians may be less likely to apply NICE guidelines to this
population and NICE guidelines may be less reliable at predicting injury within this group.

IV) **Assess the reasons adult head injury patients have for presenting after twenty-four hours of injury.**

The NSW guidelines advise treating delayed presentation head injury patients as high risk as they are likely to be a self-selecting group that have persistent symptoms, but concedes this is on the basis of a small evidence base, (New South Wales Government Ministry of Health 2012). There are a constellation of post head injury symptoms that can constitute the poorly defined clinical entity of the post-concussion syndrome (Broshek et al., 2015). The post-concussion syndrome is not associated with significant traumatic intra-cranial injury identified on CT head scan (Lannsjo et al., 2013). No previous attempts to identify the reasons head injury patients have for presenting after twenty-four hours of injury appear to have been undertaken. This has implications for the risk assessment of this group within the context of the NSW guidelines and post-concussion syndrome.

**Methods**

**Data Sources**

There were two distinct sources of routinely collected clinical data used in this study. The first was a data set of all head injury attendances to the Hull Royal Infirmary ED identified by retrospective hand searches for the period 14/11/11 to 14/5/12. A dedicated research nurse had previously undertaken hand searches of ED electronic and paper records to identify patients aged over sixteen presenting with clinical evidence of blunt head trauma, as defined by injury above the clavicles, excluding minor facial injuries or patients with penetrating head injuries. The ED records for attendance with injuries matching this definition had been photocopied and stored securely for the purposes of on going audit. There were 1592 sets of photocopied ED attendance records that had been identified and
stored in this way. This head injury patient sample included patients presenting with a head injury whether or not they underwent a CT head scan for the investigation of their injury.

The second data source was the electronic radiology requesting system. This had been used to capture all CT head requests and corresponding patient details made by the Hull Royal Infirmary Emergency Department for the time period 14/11/11 to 14/5/12. This amounted to 2240 CT head requests in this time period. This included CT head scans that were completed for reasons other than trauma. These CT head requests could be cross-referenced to both the electronic CT head reports and electronic ED notes for that specific attendance.

Figure 14 presents a summary of the process used to identify the cohorts of patients used for data extraction and analysis. Most of this analysis concentrates on the 650 patients identified using the hospital electronic requesting system as having undergone CT head imaging for the investigation of head trauma. As CT head requesting and reporting is conducted electronically through the Hull Royal Infirmary hospital network this represented a reliable method of data collection and this therefore represents a complete case series of patients that have undergone CT imaging for head trauma. The first aim of this project was to compare the prevalence of significant traumatic injuries detected by CT imaging in patients presenting within, and after, a delay in presentation. This aim was achieved by concentrating analysis on the cohort of patients that have undergone CT imaging. However, as discussed later, this limits the analysis regarding the applicability of the NICE guidelines to patients presenting after 24 hours.

However, as shown in Fig 14 and discussed later, the hand search was found to be unreliable, identifying less than half of all head injury patients that had undergone CT imaging in the 6 month period of interest. The hand search was insufficiently sensitive to identify all cases of head injury in the 6 month time period of interest. All head injury attendances associated with a CT head scan derived from the hand search were identifiable in the cohort of patient attendances derived from the electronic CT head request system.
Figure 14: Data Extraction Process From Existing Hand Search and Electronically Recorded CT requests

- **2240 CT Head Scan Requests Recorded Electronically**
  - 1318 requests clearly not for adult head trauma- identified by scanning request details
  - **922 potential CT Head Scans for adult head trauma**
    - 250 requests found not to be for adult head trauma when matched to notes
  - **672 CT Head Scans for adult head trauma**
    - 22 requests matched to incomplete notes and therefore not included in final analysis
    - **650 included CT Head Scans for adult head trauma matched to ED Notes**
      - All 296 ED CAS Card associated with a CT head request was identified in the 650 CT head scans identified from the CT head requesting system
- **1592 ED CAS Cards for head injury attendances identified by previous hand searching**
  - 53 cases not included as duplicates
  - **1539 ED CAS Cards for head injury attendances identified by hand searching**
  - **324 Attendances Associated with a completed CT Head Scan**
    - 28 ineligible as paediatric, trauma series or incomplete notes
    - **125 Attendances where injury documented as occurring greater than 24 hours before presentation**
    - **296 eligible Head injury Attendances with completed CT head scans**
      - 250 requests found not to be for adult head trauma when matched to notes
      - **672 CT Head Scans for adult head trauma**
        - 22 requests matched to incomplete notes and therefore not included in final analysis
        - **650 included CT Head Scans for adult head trauma matched to ED Notes**
      - All 296 ED CAS Card associated with a CT head request was identified in the 650 CT head scans identified from the CT head requesting system

- **650 included CT Head Scans for adult head trauma matched to ED Notes**
Data Extraction from head injury attendances identified by hand searches

The first stage of data extraction was checking and cleaning the 1592 sets of ED records previously identified by hand searches. This dataset was checked for duplicates, paediatric records and attendances not for the sole investigation of head injury. This left 1539 records of attendance following a head injury in this time period.

These records were then individually hand searched and cross-checked with the hospital’s electronic requesting system to identify all patient attendances that had resulted in a CT head scan to investigate patients within the sample of head injury patients identified by hand searches. A total of 324 ED attendance records for head injury were found to be associated with a CT head scan. Separately the 1539 ED records were hand searched and records where patients were clearly documented as attending after twenty-four hours of injury were identified. This included patients who had not undergone a CT head scan. A total of 125 ED records were identified for patients presenting after twenty-four hours. Data were then extracted in line with the clinical audit data extraction tool. This was an Excel spread sheet with predetermined domains for data-extraction and corresponding codes. For patients presenting after twenty-four hours, the reason reported for their presentation was also extracted. This process is shown in Figure 15.
Figure 15: Identification of attendances associated with CT head requests and patients presenting after 24 hours of Injury

Data extraction from the ED record, where necessary full patient notes, and CT head report was undertaken for: the day of presentation; age; sex; presence of intoxication; mechanism of injury; whether a ED CT head had been completed; CT findings; initial GCS; presence of a NICE high risk mechanism of injury; anti-coagulation; GCS less than 13 at initial assessment; GCS less than 15 two hours after the injury; signs of open or depressed skull fracture; signs of a basal skull fracture; post traumatic seizure; focal neurological deficit; greater than one episode of vomiting; retrograde amnesia greater than thirty minutes; post-traumatic amnesia; loss of consciousness; age greater than 65; time interval between injury and presentation to the ED; whether the attendance represented a re-attendance for the same injury; whether the patient required a neurosurgical
intervention or died as a result of their injury; and overall whether the patient had a NICE indication for a CT head scan.

Data extraction was completed primarily through ED record review and review of electronic CT head reports. Information pertaining to whether a patient had required neurosurgery or died as a result of their injuries could be obtained from electronically stored discharge letters and death certificates. Where data extraction from these sources was not possible, the patient’s case notes were reviewed. The absence of an individual NICE indication, for example loss of consciousness being documented, was interpreted as the absence of a NICE indication. A neurosurgical intervention was defined as any kind of invasive procedure, including intubation, intra-cranial pressure monitoring and any form of surgery related to the injury. Patients who had sustained head injuries due to a collapse were interpreted as having sustained an injury through a mechanism of a fall from standing height. A collapse was not interpreted as representing a loss of consciousness due to the head injury.

Time of presentation from the injury was divided into time groups: 0-8 hours; 9-24 hours; 25-48 hours; 49-72 hours; 73-96 hours; day 5; day 6; day 7; and greater than 1 week following the injury. This information was derived from that recorded in the ED notes, both photocopied and available electronically, and electronic request data. Time of injury was sometimes recorded precisely in the ED notes. More often it was described in general terms such as: ‘this morning’; ‘this pm’; or ‘yesterday’. Where this was the case, the patient was placed in a time grouping calculated from the time of presentation. Time of presentation for those presenting after twenty-four hours was generally easy to discern as being greater than twenty-four hours. However, the exact timing was difficult to allocate precisely and a degree of estimation was required. If a patient was stated to have sustained an injury 3 days ago it was taken as being sustained 72 hours previously. Where it was impossible to discern the time of presentation following a head injury the head injury attendance was excluded from final analysis and is counted as having been excluded from analysis due to incomplete notes. CT head
findings were only counted for analysis if they represented new traumatic abnormalities. For instance, the finding of a stroke or old traumatic pathology were not counted as a relevant abnormal radiological finding on the CT head scan and therefore did not count as a positive scan for the analysis.

Final Inclusion

A total of 324 ED records of the 1539 photocopied ED attendances for head injury were identified as being associated with a CT head scan. To be included in the final analysis the CT head scan had to have been completed for the sole investigation of isolated head trauma. Patients that underwent a CT head as part of a trauma series were excluded. Of these 296 CT head scans were included in the final analysis. Seven had incomplete notes, so data extraction including time of presentation was not possible. Similarly data extraction was not completed for four patients who were sixteen, so counted as paediatric, eleven who were requested as part of poly-trauma and three CT scans which were requested for a reason unrelated to the head injury.

As outlined previously the data set of 1539 captured Emergency Department attendances for head injury was also used to estimate the proportion of patients who attended after twenty-four hours. The photocopied ED notes were hand searched to identify all attendances where the patient was attending more than twenty-four hours following their injury. Data extraction was undertaken for 125 ED attendances all of which were included in the final analysis. Data were extracted as outlined for both groups to an excel data base saved on a password protected Emergency Department Domain of the Hull Royal Infirmary computer database for the purposes of audit. The data was then anonymised and converted to an SPSS file prior to analysis.
Patients identified by the electronic request system

For the same 6 month period of 14/11/11 to 14/5/12 that hand searches for attendances for head injury had been conducted, the department had a record of all CT head requests from the Hull Royal Infirmary Emergency Department. This included the hospital number of each patient and the corresponding CT head request for clinical data. This amounted to 2240 CT head requests in this time period. Requests that were obviously not for isolated head trauma were then removed. These included: requests from the stroke team, or that queried a stroke; requests for the investigation of a spontaneous headache not associated with trauma; or that queried a spontaneous intra-cranial haemorrhage; requests for the investigation of seizures where the seizure did not occur in conjunction with a head injury; requests for the investigation of possible space occupying lesions; requests for possible intra-cranial infection; requests for the investigation of loss of consciousness unrelated to head trauma; requests post cardiac arrest; requests for poly-trauma; and requests clearly for those under sixteen years of age. Eighty requests had no corresponding request information and these were assumed to have been requested in error and therefore were not included. The process used to identify CT head requests for the investigation of adult head trauma is shown in Figure 16.
This left 922 CT head requests potentially for the sole investigation of adult head trauma. The hospital numbers attached to these requests were used to access the electronically stored Emergency department records associated with each CT head request. The notes were then assessed for data extraction relating to the criteria outlined previously, including time of presentation from injury. Where the record indicated that the CT head request was not undertaken for the primary investigation of head trauma, data was not extracted. On matching the CT requests to the ED notes a further 250 requests were found not to be for the investigation of head trauma.
Of the 672 eligible identified completed CT head scans matched to ED records of patient attendances, only 650 were used in the final analysis. This was because 22 matched records were incomplete and this prevented data extraction. As shown in Figure 14, all 296 attendances associated with CT head scans identified in the cohort of patients derived from the previously undertaken hand search were also identifiable in 650 patient attendances derived from the electronic reporting system. The sole use of head injury patients identified by the hand search would have failed to identify 354 patient attendances associated with CT head request that were eligible for inclusion in analysis.

In each of these cases the associated electronic ED notes, electronic reports and, where necessary, full case notes, underwent data extraction as previously outlined and in line with the clinical audit data extraction tool to an Excel spread sheet. This Excel database was stored on the Hull Royal Infirmary computer network in a password protected Emergency Department domain used for the storage of audit data. This database was anonymised and converted to SPSS prior to analysis for this project.

### Statistical Analysis

IBM SPSS version 22 was used to undertake statistical analysis of the extracted data. The 95% confidence intervals for proportions are generally calculated by using the method \( p + 1.96 \sqrt{p(1-p)/n} \). However for the sensitivities of the NICE guidelines, the 95% C.I. are not calculated on the basis of Gaussian distribution due to the low number of outcomes. Instead, the confidence intervals are calculated by the method advocated by Wilson in Newcomb’s paper relating to the calculation of confidence intervals for proportions (Newcombe, 1998) using the online statistical calculator vassarstats (http://vassarstats.net/clin1.html). Pearson Chi-Square is used to test for association between dichotomous outcomes and Fishers Exact test is used when the conditions for Pearson Chi-Square are not met and less then 80% of expected frequencies exceed five. T-tests and one-way
ANOVA was used to compare the means of continuous data such as age in patients presenting within and after twenty-four hours of injury. The Wald method of logistic regression was used to create a predictive model for intracranial injury based on the presence of a NICE indication for a CT head and whether the injury was sustained within twenty-four hours of presentation. Statistical analysis was repeated with CT head scans associated with re-attendances excluded. This was to test whether the higher rate of re-attenders presenting after twenty-four hours was acting as a confounding factor, as they potentially represent an independent high-risk group, unaccounted for by NICE guidelines.

**Research Ethics**

The key ethical issue in this component of the project was the use of routinely collected clinical data, which included patient identifiable information. As a clinician working in the Emergency Department at the Hull Royal Infirmary I was auditing this data, along with other clinicians, against the national NICE guidelines. These outline the standards for management of patients with head injury in the UK. This involved compiling an electronic database of all patients who had had a CT scan in the relevant six-month period. This database included the indication for the scan, the results, basic demographic information and clinical outcome from patient notes and electronic records. Clinical audit is part of my job as an emergency department doctor based in Hull Royal Infirmary and requires no specific ethical approval. Local approval for the audit had already been given. Time of presentation following a head injury was felt to be within the remit of information that would be collected as part of clinical audit.

However some aspects of this project posed research questions as defined by the Health Research Authority: “research means to attempt to derive generalisable new knowledge by addressing clearly defined questions with systematic and rigorous methods”. The Hull and East Yorkshire Trust research and development office were consulted. They felt that this project lay at the interface between research and audit. That data collection occurring for audit was also being used to
answer research questions. Health Research Authority guidelines are that anonymised data can be used for secondary research purposes without formal ethical review. A formal IRAS application was made for the use of this data set, in this project, to answer the specific questions outlined above.

The NHS research and ethics committee that reviewed this IRAS application wrote back to state that formal NHS REC review was not required. They were satisfied that “the research is limited to the secondary use of information previously collected in the course of normal care”. Further, “the identifiable data will be collected by the clinical care team and anonymised, for the purposes of the research, for the research team”. Notably, they were satisfied that, in my capacity as a Hull Royal Emergency Department doctor already auditing these data, I qualified as part of the clinical care team The letter is included in appendix 3. This and further paper work was registered with the Research and Development Office at Hull and East Yorkshire NHS Trust and they were happy for the project to proceed. In addition to this, details of the project, as well as the research and ethics committee findings, were forwarded to the chair of Hull York Medical School ethics committee. They were satisfied that a Medical School Ethics Committee review was not necessary.

Results

What proportion of patients present after twenty-four hours following a head injury?

Hand searches of the photocopied case notes for attendance to the ED following a head injury in the six-month period 14/11/11 to 14/5/12 revealed 125 patients were documented as presenting after twenty-four hours. This represents 8.1% (95% C.I. 6.7%-9.6%) of the 1539 attendances for patients over sixteen years of age presenting with head injury. This may represent an underestimate of the number of patients who present after twenty-four hours, as clinicians may not
have recorded the time of presentation since injury in the notes of all patients. Case note reviews have been noted to underestimate the events that occur within consultations due to clinical notes being incomplete (Shah et al., 2010).

What proportion of CT head scans that are requested for patients with head injury are requested for those who present after twenty-four hours of injury?

A total of 650 CT head scans were requested as identified through the CT request system and correlated against CT heads requested for patients that were identified through hand searches. Of the 650 head scans identified, 101 were requested for patients presenting after twenty-four hours. This amounted to 15.5% (95% C.I. 12.7%-18.3%) of the total CT head requests.

There is a disparity in the proportion of patients identified as presenting after 24 hours that underwent CT imaging identified through the electronic requesting system (15.5%) and the proportion of head injury patients that present after 24 hours, irrespective of whether they underwent imaging, identified from the hand search (8.1%). To assess whether this was due to systematic selection biases in the hand search the demographics of the 296 cases of head injury associated with a CT scan derived from the hand search were compared with the 650 CT head scans associated with a head injury attendance derived the electronic requesting system. The results are summarised in table 4 below.
Table 4: Comparison of patients identified through the hand search and electronic request system

<table>
<thead>
<tr>
<th>Factor</th>
<th>650 Patients identified through electronic CT request system</th>
<th>296 patients undergone CT imaging derived from hand search</th>
<th>Chi Squared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>53.0 (51.2-54.9)</td>
<td>51.3 (48.6-54.1)</td>
<td>P=0.3 (Unpaired t-test)</td>
</tr>
<tr>
<td>Sex (% Male)</td>
<td>N=394 60.6% (56.8-64.4%)</td>
<td>N=192 64.9% (59.5-70.3%)</td>
<td>P=0.2</td>
</tr>
<tr>
<td>Initial GCS 13,14 or 15</td>
<td>N=620 95.4% (93.8-97.0%)</td>
<td>N=279 94.3% (91.7-96.9%)</td>
<td>P=0.5</td>
</tr>
<tr>
<td>Re-attendance</td>
<td>N=17 2.6% (1.4-3.8%)</td>
<td>N=7 2.4% (0.7-4.1%)</td>
<td>P=0.8</td>
</tr>
<tr>
<td>Presentation after 24 hours</td>
<td>N=101 15.5% 12.7%-18.3%</td>
<td>N=34 11.5% (7.9-15.1%)</td>
<td>P=0.1</td>
</tr>
<tr>
<td>NICE indication CT head Scan</td>
<td>N=536 82.5% (79.6-85.4%)</td>
<td>N=250 84.5% (80.4-88.6%)</td>
<td>P=0.4</td>
</tr>
</tbody>
</table>

There does not appear to be any significant differences in the characteristic of patients that have undergone CT imaging identified in the electronic requesting system and those that are also present in the hand search. Therefore, there is evidence that the hand search was a representative sample of head injury patients. The disparity in the 8.1% of head injury attendances identified from the hand search as being for patients presenting after 24 hours and the 15.5% of CT scans completed for patients presenting after 24 hours probably reflects 2 factors. The first is that clinicians may be more likely to request CT imaging for patients that present after 24 hours due to uncertainty regarding the risks of significant injury in this group. Secondly, patients that underwent CT imaging could be more readily identifiable as presenting after 24 hours due to additional available information. The electronic CT head requests details could include time of presentation from injury, even when this was not documented in the case notes.
What is the risk of significant intra-cranial injury identified by CT head imaging in patients presenting within, and after, 24 hours of injury?

Table 5 below presents the key comparisons between the non-delayed and delayed presentation head injury patient cohorts that had undergone a CT head scan (650). The overall rate of injury for patients presenting before twenty-four hours was 8.4% (95%C.I. 6.1%-10.7%) compared to 9.9% (95%C.I. 4.1%-15.7%) for non-delayed presentation patients. The difference in the proportion of patients with intra-cranial injuries presenting within and after twenty-four hours of injury was not statistically significant ($x^2$(1)=0.25, p=0.62). The frequencies of the specific types of intra-cranial injury identified are available in appendix 4.

Table 5: Comparison in rate of injury between patients presenting within and after 24 hours of injury. (95% C.I. in brackets)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Overall N=56</th>
<th>Within 24 hours N=46</th>
<th>After 24 hours N=10</th>
<th>Chi Squared/Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic CT finding</td>
<td>8.6% (6.4-10.8%)</td>
<td>8.4% (6.1-10.7%)</td>
<td>9.9% (4.1-15.7%)</td>
<td>P=0.62</td>
</tr>
<tr>
<td>Neurosurgical intervention</td>
<td>1.2%</td>
<td>0.9%</td>
<td>3%</td>
<td>P=0.11*</td>
</tr>
<tr>
<td>Death</td>
<td>0.3%</td>
<td>0.2%</td>
<td>1%</td>
<td>P=0.29*</td>
</tr>
</tbody>
</table>
Patients that re-attend following head injury have previously been identified as high risk (Voss et al., 1995). Re-attending patients were more likely to present after twenty-four hours of injury with 16/17 re-attending patients presenting again after twenty-four hours of injury. In addition to this re-attending patients appear to be a high-risk group with 4/17 re-attending patients having significant intra-cranial injuries. Therefore, this analysis was repeated but with re-attending patients excluded. This is presented in table 6 below. When this analysis was repeated the proportion of patients presenting within twenty-four hours with significant intracranial injuries was 8.4% (95% C.I. 6.1%-10.7%) and for patients presenting after twenty-four hours this proportion was 7.1% (95% C.I. 1.2%-13%). The difference in the proportion of patients with intra-cranial injuries presenting within and after twenty-four hours of injury remained statistically insignificant: $x^2(1)=0.17, p=0.68$.

Table 6: Comparison of outcomes for patients presenting within and after 24 hours of injury, with CT head scans for re-attendances removed (95% C.I. in brackets).

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trumatic CT finding</td>
<td>N=52</td>
<td>N=46</td>
<td>N=6</td>
<td>P=0.68</td>
</tr>
<tr>
<td></td>
<td>8.2% (6.1-10.8%)</td>
<td>8.4% (6.1-10.7%)</td>
<td>7.1% (1.2-13.0%)</td>
<td></td>
</tr>
<tr>
<td>Neurosurgical intervention</td>
<td>N=7</td>
<td>N=5</td>
<td>N=2</td>
<td>P=0.24*</td>
</tr>
<tr>
<td></td>
<td>1.1%</td>
<td>0.9%</td>
<td>2.4%</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>N=1</td>
<td>N=1</td>
<td>N=0</td>
<td>P=0.87*</td>
</tr>
<tr>
<td></td>
<td>0.2%</td>
<td>0.2%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>
The estimated rate of intra-cranial injury was comparable in the two groups. However the total numbers of injury and of patients presenting after twenty-four hours is low. This renders the sample underpowered for detecting all but very large differences in the proportion of injury in the groups. Given the proportion of patients that present after twenty-four hours of injury, and the rate of injury in patients presenting within twenty-four hours of injury, a sample size of 862 patient attendances would be required to find a rate of injury of 1% in patients presenting after twenty-four hours of injury as being statistically significant different to the rate of injury in patients presenting within twenty-four hours of injury (Calculated using G power 3, Faul et al., 2007).

The relative risk of injury after twenty-four hours is 1.2 (95% C.I. 0.4-2.6). When re-attenders are excluded, the relative risk of injury after twenty-four hours is 0.84 (95% C.I. 0.1-2.1). Significantly, the rate of injury is higher in patients presenting after twenty-four hours of injury when re-attenders are included in the analysis. This would suggest, as previously found, that re-attenders are a high-risk group and additionally account for a significant proportion of intra-cranial pathology in patients presenting after twenty-four hours of injury.
Table 7: Comparison of characteristic between patients presenting within 
and after 24 hours of injury (95% C.I. given in brackets)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>53.0</td>
<td>53.5</td>
<td>50.4</td>
<td>P=0.23 (anova)</td>
</tr>
<tr>
<td></td>
<td>(51.2-54.9)</td>
<td>(51.5-55.5)</td>
<td>(45.8-54.9)</td>
<td></td>
</tr>
<tr>
<td>Sex (% Male)</td>
<td>N=394</td>
<td>N=346</td>
<td>N=48</td>
<td>P&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>60.6%</td>
<td>63.0%</td>
<td>47.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(56.8-64.4%)</td>
<td>(59.0-67.0%)</td>
<td>(37.8-57.2%)</td>
<td></td>
</tr>
<tr>
<td>Re-attendance</td>
<td>N=17</td>
<td>N=1</td>
<td>N=16</td>
<td>P&lt; 0.01*</td>
</tr>
<tr>
<td></td>
<td>2.6%</td>
<td>0.2%</td>
<td>15.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.4-3.8%)</td>
<td>(8.7-22.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mechanism of Injury</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall</td>
<td>N=405</td>
<td>N=355</td>
<td>N=50</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>62.3%</td>
<td>64.7%</td>
<td>49.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(58.6-66.0%)</td>
<td>(60.7-68.7%)</td>
<td>(39.8-59.3%)</td>
<td></td>
</tr>
<tr>
<td>Assault</td>
<td>N=145</td>
<td>N=122</td>
<td>N=23</td>
<td>P=0.90</td>
</tr>
<tr>
<td></td>
<td>22.3%</td>
<td>22.2%</td>
<td>22.8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(19.1-25.5%)</td>
<td>(18.7-25.7%)</td>
<td>(14.6-30.1%)</td>
<td></td>
</tr>
<tr>
<td>RTC</td>
<td>N=46</td>
<td>N=37</td>
<td>N=9</td>
<td>P=0.43</td>
</tr>
<tr>
<td></td>
<td>7.1%</td>
<td>6.7%</td>
<td>8.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5.1-9.1%)</td>
<td>(4.6-8.8%)</td>
<td>(3.4-14.5%)</td>
<td></td>
</tr>
<tr>
<td>Sports</td>
<td>N=13</td>
<td>N=7</td>
<td>N=6</td>
<td>P=0.01</td>
</tr>
<tr>
<td></td>
<td>2.0%</td>
<td>1.3%</td>
<td>5.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.9-3.1%)</td>
<td>(0.4-2.3%)</td>
<td>(1.3-10.5%)</td>
<td></td>
</tr>
<tr>
<td>Accident(non-Specified)</td>
<td>N=27</td>
<td>N=14</td>
<td>N=13</td>
<td>P&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>4.2%</td>
<td>2.6%</td>
<td>12.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2.7-5.7%)</td>
<td>(1.3-3.9%)</td>
<td>(6.4-19.4%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>N=14</td>
<td>N=14</td>
<td>N=0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.2%</td>
<td>2.6%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1.1-3.3%)</td>
<td>(1.3-3.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 8: Comparison of characteristic between patients presenting within and after 24 hours of injury (95% C.I. given in brackets)

<table>
<thead>
<tr>
<th>Presence of risk factor</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intoxicated at time of injury</td>
<td>N=235 36.2% (32.5-39.9%)</td>
<td>N=227 41.3% (37.2-45.4%)</td>
<td>N=8 7.9% (2.6-13.2%)</td>
<td>P≤ 0.01</td>
</tr>
<tr>
<td>Dangerous Mechanism</td>
<td>N=82 12.6% (10.1-15.2%)</td>
<td>N=77 14.0% (11.1-16.9%)</td>
<td>N=5 5.0% (0.8-9.3%)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Retrograde Amnesia greater 30 mins</td>
<td>N=101 15.5% (12.7-18.3%)</td>
<td>N=100 18.2% (15.0-21.4%)</td>
<td>N=1 1.0%</td>
<td>P≤ 0.01</td>
</tr>
<tr>
<td>Post-traumatic amnesia</td>
<td>N=282 43.4% (39.6-47.2%)</td>
<td>N=266 48.5% (44.3-52.7%)</td>
<td>N=16 15.6% (8.7-22.9%)</td>
<td>P≤ 0.01</td>
</tr>
<tr>
<td>LOC</td>
<td>N=270 41.5% (37.7-45.3%)</td>
<td>N=241 43.9% (39.8-48.1%)</td>
<td>N=29 28.7% (19.9-37.5%)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Vomiting</td>
<td>N=115 17.7% (14.9-20.6%)</td>
<td>N=87 15.8% (12.8-18.9%)</td>
<td>N=28 27.7% (19.0-36.4%)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Signs of Basal Skull fracture</td>
<td>N=25 3.8% (2.3-5.3%)</td>
<td>N=22 4.0% (2.4-5.6%)</td>
<td>N=3 3.0%</td>
<td>P=0.80*</td>
</tr>
<tr>
<td>Signs of depressed Skull fracture</td>
<td>N=21 3.2% (1.9-4.6%)</td>
<td>N=17 3.1% (1.7-4.6%)</td>
<td>N=4 4.0% (0.2-7.8%)</td>
<td>P=0.55*</td>
</tr>
<tr>
<td>Seizure</td>
<td>N=24 3.7% (2.3-5.2%)</td>
<td>N=15 2.7% (1.3-4.1%)</td>
<td>N=9 8.9% (3.4-14.5%)</td>
<td>P=0.01*</td>
</tr>
<tr>
<td>Focal Neurological Deficit</td>
<td>N=34 5.2% (3.5-6.9%)</td>
<td>N=23 4.2% (2.5-5.9%)</td>
<td>N=11 10.9% (4.9-17.0%)</td>
<td>P=0.01</td>
</tr>
</tbody>
</table>

Table 7 and 8, above, summarises the key differences in demographics, mechanism of injury and presence of NICE indications for a CT head scan in those presenting within, and after, twenty-four hours of a head injury. Notably, significantly more males present within twenty-four hours of injury. There are also significant differences in the reported mechanisms of injury and the presence of individual NICE indications for a CT head scan in the two groups. The significance of these differences as potential confounding factors is discussed later in this chapter, along with other potential limitations of this study.
Are NICE Guidelines utilised as much and as sensitive for patients presenting after twenty-four hours of injury?

The proportion of patients that presented within twenty-four hours that had a CT head scan, when no NICE indication was present, was 75/549 = 13.7% (95% C.I. 10.8%-16.6%). After twenty-four hours the proportion of CT head scans conducted, when no NICE indication was present, increased to 39/101 = 38.6% (95% C.I. 29.1%-48.1%). This is a statistically significant difference (\(x^2(1) = 36.73, p \leq 0.01\)). This is presented in the Table 9.

Table 9: Presence of a NICE indication for CT head scan, stratified by time of presentation

<table>
<thead>
<tr>
<th></th>
<th>CT Scan when NICE +VE</th>
<th>CT Scan when NICE -VE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation Within 24 Hours</td>
<td>474 (86.3%)</td>
<td>75 (13.7%)</td>
<td>549</td>
</tr>
<tr>
<td></td>
<td>(95% C.I. 83.4%-89.2%)</td>
<td>(95% C.I. 10.8%-16.6%)</td>
<td></td>
</tr>
<tr>
<td>Presentation After 24 Hours</td>
<td>62 (61.4%)</td>
<td>39 (38.6%)</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>(95% C.I. 51.9%-70.9%)</td>
<td>(95% C.I. 29.1%-48.1%)</td>
<td></td>
</tr>
</tbody>
</table>

The relative risk of having a CT head for a non-NICE indication after twenty-four hours was 2.8 (95% C.I. 1.75%-4.5%). Presenting after twenty-four hours significantly increased the chance of having a CT head scan when no NICE indication was present. This implied that clinicians appear to regard NICE guidelines as being less reliable at predicting which patients had traumatic intracranial injuries after in patients presenting after twenty-four hours of injury. The analysis was repeated excluding re-attendances as this represents an established high-risk group who clinicians may be more likely to investigate with a CT head scan in the absence of a NICE indication. This repeat analysis found the relative risk for having a CT head when NICE “negative” for patients presenting after twenty-four hours of injury to be 3.1 (95% C.I. 1.8%-4.9%). This shows that the
relative chance of having a CT head scan when there was no NICE indication for patients presenting after twenty-four hours, increased when re-attenders were excluded from the analysis. This indicates that the increased rate of CT for NICE negative patients, in patients presenting after twenty-four hours of injury, is not due to the confounding effect re-attending patients. Instead, it shows that clinicians regard non-NICE indications as potential predictors of intra-cranial injury in patients presenting more than twenty-four after their injury.

The sensitivity of the NICE guidelines is a measure of the proportion of significant intra-cranial injuries and neurosurgical outcomes the guidelines identify. Overall, the NICE guidelines were predictive of 52/56 intra-cranial injuries and 9/10 injuries that resulted in neurosurgery or death. This corresponds to a 92.9% sensitivity (95% C.I. 81.9%–97.7%) for traumatic intra-cranial pathology identified on CT and a 90% sensitivity (95% C.I. 54.1%–99.5%) for neurosurgical outcome or death. This analysis was repeated but stratified by presentation within and after twenty-four hours. Table 10 presents these data:

Table 10: The sensitivity of the NICE guidelines in intra-cranial injuries, neurosurgery and death

<table>
<thead>
<tr>
<th></th>
<th>NICE +VE</th>
<th>NICE–VE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-cranial Injury</strong></td>
<td>52</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td><strong>Neurosurgery or Death</strong></td>
<td>9</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td><strong>Patients presenting within 24 hours</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-cranial Injury</td>
<td>45</td>
<td>1</td>
<td>46</td>
</tr>
<tr>
<td>Neurosurgery or Death</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td><strong>Patients Presenting after 24 hours</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-cranial Injury</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Neurosurgery or Death</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>
The sensitivity of NICE guidelines for traumatic intra-cranial findings on CT was 97.8% (95% C.I. 87%-99.9%) predicting 45/46 injuries and 100% (51.7-100%) sensitive for neurosurgical outcomes or death predicting all such outcomes within twenty-four hours. For patients presenting after twenty-four hours, the NICE guidelines predicted 7/10 injuries equating to 70% (95% C.I. 35.4%-91.9%) sensitivity and predicted 3/4 neurosurgical outcomes or deaths. This corresponds to a sensitivity of 75% (95% C.I. 21.9%-98.8%). A sensitivity of 75% is evidence that the NICE guidelines are less sensitive and effective at predicting injury in patients presenting after twenty-four hours. Repeating the analysis with re-attenders, excluded to prevent the confounding effect of an established high-risk group, (Voss et al., 1995) does not alter this finding. The NICE guidelines would have predicted 4/6 injuries equating to a sensitivity of 66.7% (95% C.I. 24.1%-94%) in patients presenting after twenty-four hours when re-attenders are excluded. The sensitivity is unchanged in patients presenting within twenty-four hours. The key difference is that the NICE guidelines would have predicted all neurosurgical outcomes or deaths in both groups and would therefore have had 100% sensitivity for these outcomes.

Data were stratified as shown below to further investigate the relationship between: time of presentation; the presence of a NICE indication for a CT head scan following a head injury (Table 11); and intra-cranial injury (Table 12 and 13). Pearson Chi-squared and Fisher’s Exact test were used to test whether the presence of a NICE indication for the completed CT head scans was associated with traumatic abnormal findings.
Table 11: Risk of intra-cranial injury in the presence and absence of a NICE indication for a CT head scan

<table>
<thead>
<tr>
<th>Overall</th>
<th>NICE Indication for CT Head</th>
<th>No NICE indication for CT head</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-cranial Injury</td>
<td>52</td>
<td>4</td>
</tr>
<tr>
<td>No Intra-cranial Injury</td>
<td>484</td>
<td>110</td>
</tr>
</tbody>
</table>

| Risk of intra-cranial Injury | 9.7% (95% C.I. 7.2%-12.2%) | 3.4% (95% C.I. 0.01%-6.7%) |

(\(x^2(1)\) 4.58, \(p=0.03\))

Table 12: Risk of intra-cranial injury in the presence and absence of a NICE indication for a CT head scan in patients presenting within 24 hours of injury

<table>
<thead>
<tr>
<th>Patients Presenting within 24 hours</th>
<th>NICE Indication for CT Head</th>
<th>No NICE indication for CT head</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-cranial Injury</td>
<td>45</td>
<td>1</td>
</tr>
<tr>
<td>No Intra-cranial Injury</td>
<td>429</td>
<td>74</td>
</tr>
</tbody>
</table>

| Risk of intra-cranial Injury | 9.5% (95% C.I. 6.9%-12.1%) | 1.3% (95% CI: 0.0%-3.9%) |

(\(x^2(1)\) 5.62, \(p=0.02\))
Table 13: Risk of intra-cranial injury in the presence and absence of a NICE indication for a CT head scan in patients presenting after 24 hours of injury

<table>
<thead>
<tr>
<th>Patients Presenting after 24 hours</th>
<th>NICE Indication for CT Head</th>
<th>No NICE indication for CT head</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-cranial Injury</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>No Intra-cranial Injury</td>
<td>55</td>
<td>36</td>
</tr>
<tr>
<td>Risk of intra-cranial Injury</td>
<td>11.3% (95% CI: 3.4% - 19.2%)</td>
<td>7.7% (95% CI: 0.7% - 16.1%)</td>
</tr>
</tbody>
</table>

The presence of a NICE indication for a CT head scan is associated with traumatic intra-cranial injuries in those presenting within twenty-four hours (p=0.02), but not in those presenting after twenty-four hours of injury (p=0.74). Hence, there is evidence of association between the presence of intra-cranial injuries and a NICE indication for a CT head scan for those presenting within twenty-four hours of their injury, but not for those presenting later.

When analysis was repeated with CT head scan associated with re-attending patients excluded this finding remained. There remained overall evidence of association between the presence of a NICE indication for a CT head scan and with traumatic intra-cranial injuries (P=0.02). Stratification by time of presentation showed that within twenty-four hours this association remained (P=0.02). After twenty-four hours there was no evidence of association between the presence of a NICE indication and CT head abnormalities (P=0.52).

Logistic regression was used to explore the relationship between the presence of a NICE indication for a CT head scan, presentation after twenty-four hours of injury and traumatic intra-cranial CT head abnormalities. The following model was created using the Wald method of logistic regression: Log (Odds Abnormal CT)=
Coefficient (Presence NICE Indication) + Coefficient (presentation after 24 hours) + constant.

In this model presence of a NICE indication predicted abnormal traumatic findings (p=0.03), whilst whether presentation occurred after twenty-four hours of injury did not (p=0.28). The Hosmer-Lemeshow Goodness of Fit Test has an associated P value of 0.38, which indicates a good fit between this regression model and observed values. The components of this model are presented in Table 14. These findings are consistent with the previous findings that the NICE guidelines are generally predictive of injury and that the incidence of intra-cranial injury in patients presenting within, and after, twenty-four hours of injury are comparable.

It is possible to model K factors in a logistic regression model as determined by \(N=10k/P\), where \(N\) is the number of data points and \(P\) is the proportion of outcomes (Stoltzfus, 2011). As there are 650 data points in this data set, and the prevalence of intracranial injury was 8.6%, then up to five potential explanatory variables could have been investigated.

**Table 14: Components of logistic regression model for traumatic intra-cranial CT head abnormality**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Co-efficient</th>
<th>Wald</th>
<th>Sig</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE Indication</td>
<td>1.19</td>
<td>4.83</td>
<td>p=0.03</td>
<td>3.30 (95% C.I. 1.14-9.46)</td>
</tr>
<tr>
<td>Presentation after 24 hours</td>
<td>0.41</td>
<td>1.19</td>
<td>p=0.28</td>
<td>1.51 (95% C.I. 0.72-3.17)</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.47</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The interaction between the presence of a NICE indication for a CT head scan and presentation after twenty-four hours of injury was explored. The results are presented in Table 15:

Table 15: interactivity between presentation after 24 hours of injury and a NICE indication for a CT head scan

<table>
<thead>
<tr>
<th>Factor</th>
<th>Co-efficient</th>
<th>Wald</th>
<th>Sig</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE Indication</td>
<td>2.05</td>
<td>4.0</td>
<td>p=0.04</td>
<td>7.76 (95% C.I. 1.05-57.18)</td>
</tr>
<tr>
<td>Presentation after 24 hours</td>
<td>1.82</td>
<td>2.41</td>
<td>p=0.12</td>
<td>6.17 (95% C.I. 0.62-61.38)</td>
</tr>
<tr>
<td>NICE indication * presentation after 24 hours</td>
<td>-1.63</td>
<td>1.69</td>
<td>p=0.19</td>
<td>0.20 (95% C.I. 0.2-2.28)</td>
</tr>
<tr>
<td>Constant</td>
<td>-4.30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This demonstrates that when interaction is controlled for, the odds ratio of having an intracranial injury when a NICE indication is present increases from 3.30 to 7.76. The presence of a NICE indication remains statistically predictive of intra-cranial injury (p=0.04). When a NICE indication is present and presentation is after twenty-four hours, this is found to negatively predict intra-cranial injury but not statistically significantly so (p=0.19). Therefore, for patients presenting after twenty-four hours of injury the presence of a NICE indication for a CT head scan is found not to be predictive of intra-cranial injuries.

To explore this further the logistic regression model was stratified by whether the patient presented within or after twenty-four hours of their injury. Table 16 below presents a summary of this. The findings indicate that for patients presenting within twenty-four hours of injury the presence of a NICE indication for a CT
head scan statistically predicts intra-cranial pathology (p=0.04), but does not do so for patients resenting after this (p=0.56).

**Table 16: logistic regression model stratified by time of presentation**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Factor</th>
<th>Co-efficient</th>
<th>Wald</th>
<th>Sig</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 24 hours</td>
<td>NICE Indication</td>
<td>2.05</td>
<td>4.05</td>
<td>p=0.04</td>
<td>7.76 (95% C.I. 1.05-57.18)</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>-4.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 24 Hours</td>
<td>NICE Indication</td>
<td>0.42</td>
<td>0.34</td>
<td>P=0.56</td>
<td>1.53 (95% C.I. 0.37-6.30)</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>-2.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The odds of having an abnormal CT head when a NICE indication is present are almost 8 times greater for patients presenting within twenty-four hours of injury as compared to only 1.5 times for patients presenting after twenty-four hours of injury. Only 101 CT head scans were completed for patients presenting after twenty-four hours of injury. However, the proportion of intra-cranial injuries in this group was 9.9%, therefore given it is possible to model K explanatory variables in the equation N=10k/p, this group is just large enough to power this logistic regression model (Stoltzfus, 2011).

This logistic regression modelling was repeated with re-attending patients excluded to test for their potential confounding effect. For patients presenting within twenty-four hours the presence of a NICE indication for a CT head remained predictive of intra-cranial injury (p=0.05). For patients presenting after twenty-four hours, the presence of a NICE indication for a CT head remained
non-predictive of intra-cranial injury (p=0.69). The results are summarised in the table 17 below:

**Table 17: Logistic regression model with CT head scans for re-attending patients excluded from analysis**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Factor</th>
<th>Co-efficient</th>
<th>Wald</th>
<th>Sig</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Within 24 hours</td>
<td>NICE Indication</td>
<td>2</td>
<td>4</td>
<td>p=0.05</td>
<td>7.7 (95% C.I. 1.04-56.42)</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>-4.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After 24 Hours</td>
<td>NICE Indication</td>
<td>0.36</td>
<td>0.162</td>
<td>p=0.69</td>
<td>1.4 (95% C.I. 0.25-8.30)</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>-2.8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall, clinicians are significantly more likely to request CT head scans for patients where NICE indications are not present when patients present after twenty-four hours of their injury. The NICE guidelines appeared highly sensitive for intra-cranial injuries in patients presenting within twenty-four hours of injury with statistical association between the presence of a NICE indication and CT abnormalities within this group. In patients presenting after twenty-four hours of their injury the NICE guidelines are less sensitive and no statistical association was found between the presence of a NICE indication and CT abnormalities. The difference in the performance of the NICE guidelines in patients presenting within, and after, twenty-four hours of injury does not appear to be due to the higher proportion or re-attending patients presenting after twenty-four hours of injury.

**Why do patients present after twenty-four hours?**

The hand search of the data set of photocopied notes for all head injury attendances, identified through retrospective hand searching of ED attendances
from November 2011- April 2012, revealed 125 attendances for patients where it was clearly documented that the head injury had been sustained more than twenty-four hours previously. The reason for the patient attending the ED, as recorded in the notes, was extracted. The results are summarised in table 18. It also shows what proportion of patients in each symptom group present in the different time intervals.

Notably, headache is the most common single reason for patients to present after twenty-four hours following a head injury. Patients present with a headache in almost all time-delay intervals, including more than a week following a head injury. As discussed previously, headache was not identified as a risk factor for intra-cranial injury on CT or neurosurgery in the CCHR study, but was identified as a risk factor in the New Orleans study (Haydel et al., 2000, Stiell et al., 2001). Headache is not part of the NICE indications for a CT head following a head injury, yet the significance of a persistent headache after twenty-four hours of the injury is unknown (NICE, 2014). It may represent a benign common post head injury phenomenon (Lieba-Samal et al., 2011). However, an ED head injury specialist, who was consulted in the formulation of the clinical vignettes, advocated a CT head for all delayed presentation head injury patients presenting with a headache as this may represent a slowly accumulating intra-cranial haemorrhage. This is a clinical position also taken by the NSW head injury guidelines (New South Wales Government Ministry of Health, 2012).
### Table 18: Reasons for patients attending after twenty-four hours of injury

<table>
<thead>
<tr>
<th>Time of Present</th>
<th>Headache</th>
<th>Headache and vomiting</th>
<th>Vomiting</th>
<th>Vomiting</th>
<th>Headache and dizziness</th>
<th>Dizziness</th>
<th>Nauseous</th>
<th>Advised by 3rd party</th>
<th>Check Over</th>
<th>Confusion</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>45 (36.0%)</td>
<td>3 (2.4)</td>
<td>5 (4.0%)</td>
<td>6 (4.8%)</td>
<td>13 (10.4%)</td>
<td>6 (4.8%)</td>
<td>12 (9.6%)</td>
<td>22 (17.7%)</td>
<td>4 (3.2%)</td>
<td>9 (7.2%)</td>
<td></td>
<td>125</td>
</tr>
<tr>
<td>24-48</td>
<td>21 (46.7%)</td>
<td>1 (33.0%)</td>
<td>3 (60.0%)</td>
<td>1 (16.7%)</td>
<td>7 (53.8%)</td>
<td>2 (33.3%)</td>
<td>4 (33.3%)</td>
<td>8 (36.4%)</td>
<td>3 (75.0%)</td>
<td>6 (66.6%)</td>
<td></td>
<td>56</td>
</tr>
<tr>
<td>49-72</td>
<td>6 (13.3%)</td>
<td>0 (0.0%)</td>
<td>1 (20.0%)</td>
<td>0 (0.0%)</td>
<td>1 (7.7%)</td>
<td>1 (16.7%)</td>
<td>1 (8.3%)</td>
<td>5 (22.7%)</td>
<td>0 (0.0%)</td>
<td>1 (11.1%)</td>
<td></td>
<td>16</td>
</tr>
<tr>
<td>73-96</td>
<td>8 (17.8%)</td>
<td>1 (20.0%)</td>
<td>2 (33.3%)</td>
<td>1 (16.7%)</td>
<td>3 (25%)</td>
<td>1 (4.5%)</td>
<td>0 (0.0%)</td>
<td>1 (11.1%)</td>
<td>19 (15.2%)</td>
<td></td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Day 5</td>
<td>3 (6.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1 (16.7%)</td>
<td>0 (0.0%)</td>
<td>1 (16.7%)</td>
<td>1 (8.3%)</td>
<td>2 (9.1%)</td>
<td>0 (0.0%)</td>
<td>1 (11.1%)</td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Day 6</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Day 7</td>
<td>1 (2.2%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>3 (25.0%)</td>
<td>2 (9.1%)</td>
<td>1 (25.0%)</td>
<td>0 (0.0%)</td>
<td>7 (5.6%)</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>More Than A week</td>
<td>6 (13.3%)</td>
<td>1 (33.0%)</td>
<td>0 (0.0%)</td>
<td>2 (33.3%)</td>
<td>4 (30.8%)</td>
<td>1 (16.7%)</td>
<td>0 (0.0%)</td>
<td>4 (18.2%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td>18</td>
</tr>
</tbody>
</table>
The second most common reason for patients to attend was for a “check over”, at the patient’s request, due to having a head injury as opposed to having a specific symptom. A proportion of patients presented to be checked over more than a week following a head injury. In addition to this 9.6% of patients attended after twenty-four hours following advice from third parties, often the police or a G.P., to attend the ED for evaluation as they had sustained a head injury. These patients collectively represent over 25% of patients presenting more than twenty-four hours after their injury and are potentially an asymptomatic group. Factors relating to the mechanism and circumstances of the initial head injury may be less relevant when risk assessing asymptomatic delayed presentation head injury patients. They may be a group where CT is less appropriate.

The final significant reasons for patients attending more than twenty-four hours following a head injury were non-specific symptoms of dizziness or nausea and feeling generally unwell. These symptoms in isolation do not form part of the CCHR, New Orleans decision rule or NICE guidelines (Haydel et al., 2000, Stiell et al., 2001, NICE, 2014). They could result from abnormal neurological function that would be identifiable in a physical examination of a patient and would represent an indication for a CT head scan in all decision rules. Alternatively, they may be part of the spectrum of symptoms found in the post-concussion syndrome. This is a syndrome of persistent symptoms unrelated to significant traumatic intra-cranial pathology that can occur in a sub-population of patients following a head injury (Ganti et al., 2014). Indeed, subjective dizziness represents one commonly cited symptom in the post-concussion syndrome (Ganti et al., 2014). The significance of these symptoms, and their persistence after twenty-four hours of injury, is not known and does not from part of the NICE guidelines. Therefore the clinical risk assessment of this group may be difficult. Symptoms such as this and persistent headache may account for the significantly higher rate of CT heads completed for non-NICE indications in patients presenting more than twenty-four hours after their injury.
Limits of the Study:

Potential Confounding Factors

Any cohort study is prone to selection bias and the effect of confounding factors that reflect systematic differences between the two groups being compared. These factors can cause the apparent differences in observed effects between the comparison groups and lead to wrongly attributing causality to the exposure being studied. In this case the exposure being studied is time of presentation and comparison groups are patients who have had a CT head scan presenting within twenty-four hours of their injury and patients presenting after twenty-four hours of their injury. The outcomes being measured are the proportion of patients with traumatic injuries as identified by CT scan and the proportion of patients who have had a scan when no NICE indication was present.

The potential confounding effect of re-attendance has been explored. Analysis with re-attenders excluded did not alter the comparative findings between patients presenting within, and after, twenty-four hours. In order to explore further potential confounding factors, data collected relating to demographics and circumstances of the injuries were compared between the groups. These key differences are presented in Table 19.
Table 19: Difference between patients presenting within and after 24 hours of injury, (95% C.I. given in brackets)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/*Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>53 (51.2-54.9)</td>
<td>53.5 (51.5-55.5)</td>
<td>50.4 (45.8-54.9)</td>
<td>P=0.23 (anova)</td>
</tr>
<tr>
<td>Sex (% Male)</td>
<td>60.6% (56.8-64.4%)</td>
<td>63.0% (59.0-67.0%)</td>
<td>47.5% (37.8-57.2%)</td>
<td>P≤0.01</td>
</tr>
<tr>
<td>Initial GCS 13,14 or 15</td>
<td>95.4% (93.8-97.0%)</td>
<td>94.9% (93.6-96.7%)</td>
<td>98.0% (95.3-100.0%)</td>
<td>*0.21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mechanism of Injury</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/*Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fall</td>
<td>62.3% (58.6-66.0%)</td>
<td>64.7% (60.7-68.7%)</td>
<td>49.5% (39.8-59.3%)</td>
<td>P=0.70*</td>
</tr>
<tr>
<td>Assault</td>
<td>22.3% (19.1-25.5%)</td>
<td>22.2% (18.7-25.7%)</td>
<td>22.8% (14.6-30.1%)</td>
<td>P=0.90</td>
</tr>
<tr>
<td>RTC</td>
<td>7.1% (5.1-9.1%)</td>
<td>6.7% (4.6-8.8%)</td>
<td>8.9% (3.4-14.5%)</td>
<td>P=0.43</td>
</tr>
<tr>
<td>Sports</td>
<td>2.0% (0.9-3.1%)</td>
<td>1.3% (0.4-2.3%)</td>
<td>5.9% (1.3-10.5%)</td>
<td>P=0.01*</td>
</tr>
<tr>
<td>Accident(non-Specified)</td>
<td>4.2% (2.7-5.7%)</td>
<td>2.6% (1.3-3.9%)</td>
<td>12.9% (6.4-19.4%)</td>
<td>P≤0.01</td>
</tr>
<tr>
<td>Unknown</td>
<td>2.2% (1.1-3.3%)</td>
<td>2.6% (1.3-3.9%)</td>
<td>0% (0-0)</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Presence of risk factor</th>
<th>Overall</th>
<th>Within 24 hours</th>
<th>After 24 hours</th>
<th>Chi Squared/*Fisher Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intoxicated at time of injury</td>
<td>36.2% (32.5-39.9%)</td>
<td>41.3% (37.2-45.4%)</td>
<td>7.9% (2.6-13.2%)</td>
<td>P≤0.01</td>
</tr>
<tr>
<td>Dangerous Mechanism</td>
<td>12.6% (10.1-15.2%)</td>
<td>14.0% (11.1-16.9%)</td>
<td>5.0% (0.8-9.3%)</td>
<td>P=0.01</td>
</tr>
<tr>
<td>Retro-grade Amnesia greater 30 mins</td>
<td>15.5% (12.7-18.3%)</td>
<td>18.2% (15.0-21.4%)</td>
<td>1.0% (0-1)</td>
<td>P≤0.01</td>
</tr>
<tr>
<td>Post-traumatic amnesia</td>
<td>43.4% (39.6-47.2%)</td>
<td>48.5% (44.3-52.7%)</td>
<td>15.8% (8.7-22.9%)</td>
<td>P≤0.01</td>
</tr>
<tr>
<td>LOC</td>
<td>41.5% (37.7-45.8%)</td>
<td>39.9% (39.8-48.1%)</td>
<td>28.7% (19.9-37.5%)</td>
<td>P=0.02</td>
</tr>
<tr>
<td>Vomiting</td>
<td>17.7% (14.8-20.6%)</td>
<td>15.0% (12.8-18.9%)</td>
<td>27.7% (19.36-34.4%)</td>
<td>P=0.78*</td>
</tr>
<tr>
<td>Signs of Basal Skull fracture</td>
<td>3.8% (2.3-5.3%)</td>
<td>4.0% (2.4-5.6%)</td>
<td>3.0% (0-6)</td>
<td>P=0.55*</td>
</tr>
<tr>
<td>Signs of depressed Skull fracture</td>
<td>3.2% (1.9-4.6%)</td>
<td>3.1% (1.7-4.6%)</td>
<td>4.0% (0.2-7.8%)</td>
<td>P=0.01*</td>
</tr>
<tr>
<td>Seizure</td>
<td>3.7% (2.3-5.2%)</td>
<td>2.7% (1.3-4.1%)</td>
<td>8.9% (3.4-14.5%)</td>
<td>P=0.01*</td>
</tr>
<tr>
<td>Focal Neurological Deficit</td>
<td>5.2% (3.5-6.9%)</td>
<td>4.2% (2.5-5.9%)</td>
<td>10.9% (4.8-17.0%)</td>
<td>P=0.01</td>
</tr>
</tbody>
</table>

Age was found to be comparable in both groups with similar means and overlapping confidence interval for age in the various groupings related to time of presentation. There is a significant difference in the proportion of males presenting within and after twenty-four hours of injury. A greater number of
males presented overall due to head injury, but a disproportionately low number presented after twenty-four hours. Sex was not identified as an independent risk factor for intra-cranial injury in the original decision rule papers (Haydel et al., 2000, Stiell et al., 2001) and does not form part of the NICE guidelines (NICE, 2014). Therefore, it is unlikely that the difference in the proportion of males in patients presenting within, and after, twenty-four hours of injury would affect the rate of injury in these two groups. However, it is not known what effect patients’ gender has on clinician assessment and application of NICE guidelines. This could have altered CT scanning practice. There does not appear to be a difference in the initial severity of injury between the two groups. A similar proportion of minor head injury patients with an initial GCS of 13 or more were present in both patients presenting within and after twenty-four hours of injury.

There is also a significant difference in the proportion of patients that were reported to be intoxicated at time of injury in those presenting within twenty-four hours of injury and those presenting after. Alcohol intoxication represents a potentially confounding factor as it has been reported previously as increasing the risk of significant intra-cranial injury following a head injury (Barrow et al., 2012). It is difficult to know whether this difference in intoxication between the two groups is true or reflects recall bias. Patients presenting within twenty-four hours are more likely to be actively intoxicated when assessed and therefore intoxication is more likely to have been recorded in the notes. Patients presenting after twenty-four hours may have denied or not actively disclosed whether they were intoxicated at the time of injury. As intoxication does not form part of the NICE guidelines, clinicians may not have actively sought information about this. Therefore, although it is necessary to acknowledge this difference as a potentially confounding factor, its impact is difficult to assess.

The mechanisms of injury were similar in the two groups with falls and assaults being the most common causes of head injuries in both. The only significant differences were that patients presenting after twenty-four hours were statistically less likely to present due to a fall and more likely to present due to an unspecified
accident. This may reflect that patients presenting after twenty-four hours may be less able to describe or explain the exact mechanism of their injury due to incomplete recall. This is a potentially large confounding factor when applying the NICE guidelines to patients presenting after twenty-four hours.

Notably, patients presenting within twenty-four hours are statistically more likely to have a NICE indication or risk factor present, which relates to the circumstances of the injury, than patients presenting after twenty-four hours of injury. This includes loss of consciousness due to the injury, amnesia as result of the injury, or presence of a dangerous mechanism of injury. This may be because a head injury resulting from a dangerous mechanism, or causing any of those immediate symptoms, may prompt urgent attendances to the ED. It may also be the case that patients presenting after twenty-four hours have incomplete recall and therefore such risk factors are not noted.

The presence of signs of skull fractures is comparable in both groups. The findings of abnormal neurology or the occurrence post-traumatic seizure is higher in the delayed presentation group, but not statistically. Vomiting, as a NICE indication, was statistically higher in the delayed-presentation group. This shows that NICE indications that relate to the circumstances of the injury are lower in the delayed-presentation group. However, NICE indications that relate to clinical examination or post-head injury symptoms are comparable, or higher, in patients presenting after twenty-four hours. These findings may be true and reflect the fact that worrying features at the time of injury are likely to cause patients to present earlier, whilst on-going symptoms cause patients to present later, or they could reflect recall bias. Therefore the apparent difference in the application and sensitivity of NICE guidelines in patients presenting after twenty-four hours could be due to incomplete patient recollection instead of true differences.
Analysis Focuses on Patients who have undergone CT Head Imaging

The main weakness in this part of the study is that most analysis has been conducted on the cohort of head injury patients that have undergone CT head imaging. The electronic requesting system is likely to have accurately captured all patients that had a CT head scan in this time period and therefore estimates about the prevalence of significant injury derived from this are likely to be accurate findings for this group. To accurately assess the prevalence of significant intra-cranial injuries in a cohort of all head injury patients and compare the prevalence of injury in patients presenting within, and after 24 hours, every patient would need to undergo CT head imaging. This would not be ethical given the radiation risk and resource implications.

The estimate of intra-cranial pathology presented is only in patients who have had a CT head scan. This will therefore be an over-estimation of prevalence of intra-cranial pathology in head injury patients as it excludes the minor head injury patients that were discharged without a CT scan. The retrospective study design means that it is not possible to know whether patients that did not undergo CT head imaging had undetected injuries. It is likely that if they did they would have clinically deteriorated and represented at Hull Royal Infirmary. However, small injuries may not have precipitated re-attendance and patients re-presenting at other hospitals may have been missed.

The overall prevalence of intra-cranial injury was found to be 8.6% (95% C.I. 6.4%-10.8%) in all head injury patients that had undergone CT head imaging. This is comparable, although higher than the reported 4.8% rate of intra-cranial haemorrhage in a population of head injury patients that had also all undergone CT head, but on the basis of the CCHR (Albers et al., 2013). The higher rate of injury reported in this study is due to the Albers paper only including GCS 14 and 15 patients and only including different kinds of intra-cranial haemorrhage as the outcome measure (Albers et al., 2013). A large systematic review appraising decision-rule studies reported a median prevalence of intra-cranial injury in the studies of 7.2% (Harnan et al., 2011). The New Orleans and CCHR studies
reported the rate of injury in minor head as 6.9% and 8% respectively (Haydel et al., 2000, Stiell et al., 2001). The rate of injury reported in this study is comparable, but again higher, as this study relates to a higher risk population and excludes patients who have not had a CT scan.

This part of the study compares the prevalence of detected intra-cranial injuries in patients that have undergone CT imaging that presented within, and after, 24 hours of injury. The objective is to assess whether patients that present after 24 hours have a different risk of injury. Such a comparison is only valid if the proportion of patients that undergo CT imaging is similar in both groups. If clinicians were less likely to CT image patients presenting after 24 hours of injury then fewer injuries may have been detected causing this group to appear to be lower risk. This would be particularly true of small intra-cranial injuries that may not necessarily cause marked clinical deterioration and re-presentation. Equally, if uncertainty regarding the risks of serious injury in delayed presentation head injury patients led to a higher baseline rate of CT imaging in this group then a greater number of less significant injuries may have been detected. This would lead to a biased and falsely elevated estimate of the prevalence of significant injury.

However, the number of deaths and neurosurgical outcomes were similar in both groups. These outcomes are unlikely to be affected by such biases as they represent the consequences of serious injuries. This supports the finding that the prevalence of significant intra-cranial injuries is similar in patients presenting within and after 24 hours of injury. Furthermore, the proportion of patients that were identified as presenting after 24 hours derived from the previously undertaken hand search that underwent CT imaging, was similar to the proportion of patients identified as presenting within 24 that underwent CT imaging: 33/125 (26.4% 95% C.I. 18.7%-34.13) patients presenting after 24 hours underwent CT imaging; and 263/1386 (19.1% 17.0-21.2% 95% C.I.) patients presenting within 24 hours underwent CT imaging.
Comparing the prevalence of detected injury in patients presenting within and after 24 hours of injury that have undergone CT imaging may not be a completely unbiased way of comparing risk of injury in these groups. However, from the available data, it appears to represent a valid comparison of risk of injury in the two groups. The prevalence of intra-cranial injury in all head injury presenting within and after 24 hours of injury, as opposed to just those that undergo CT head imaging, would as discussed previously be lower than that estimated from the cohort of patients used. However, this does not affect the key finding that patients presenting within and after 24 hours have a similar risk of injury.

**Limitations in the Evaluation of the NICE Guidelines**

Ideally to compare the performance of the NICE guidelines in patients presenting within, and after 24 hours, of injury a prospective validation study of the guidelines would have been conducted for both groups. Head injury patients that did not undergo CT head imaging would be formally followed up to ensure intra-cranial injuries were not missed. A complete cohort of all head injury patients would be used to calculate the comparative sensitivity and specificity of the NICE guidelines for patients presenting within and after 24 hours of injury. Such a study was however beyond the time and resources available for this project. The retrospective nature of the data available for this project means it is difficult to assess whether patients that did not undergo CT head imaging had significant injuries. As discussed earlier the most reliable cohort available for analysis was of head injury patients who had undergone CT head imaging.

Analysis therefore has focused on this group, however this makes the scope of the findings limited. No comment can be made on the specificity, and therefore cost effectiveness of the NICE guidelines, without including patients who have not undergone CT imaging in the analysis. The analysis also only tells half the story regarding clinicians’ use of the NICE head injury guidelines. It fails to assess what proportion of patients presenting within, and after 24 hours, of injury with a NICE indication for CT imaging did not undergo such imaging. The clinical vignette based survey found clinicians to be less likely to CT image patients with
NICE guideline indications if they presented in a delayed manner. Focusing analysis on patients that had undergone imaging meant that this was not assessed with the available real world data.

The sensitivity estimate may also be inaccurate. Due to the retrospective nature of the available data, patients with small intra-cranial injuries that failed to undergo CT imaging would have been missed. Similarly patients with more significant injuries that re-presented at different hospitals or after the 6 month period of the study may have also been missed. This is more likely to apply to patients without a guideline indication for a CT scan as these patients are less likely to undergo CT imaging, especially at first presentation. This may result in an overestimation of the sensitivity of the guidelines, especially in patients presenting within 24 hours of injury. The sensitivity analysis may also be distorted by the failure to include NICE positive patients that did not undergo CT imaging. This is unlikely to substantially affect the sensitivity of the NICE guidelines estimated for patients presenting within 24 hours of injury because previously conducted clinical audits at Hull Royal Infirmary ED indicate that over 90% of patients with a NICE indication undergo CT imaging. However, as indicated by the clinical vignette based survey, this may represent a significant number of patients presenting after 24 hours of injury. Therefore, the sensitivity of the NICE guidelines calculated for this group may be an overestimate.

**Hand Searching was found to be unreliable**

Hand searching for head injury patients was identified as an unreliable method of data collection as it identified only 296/650 eligible head-injury attendances associated with CT head imaging. This reflects that the hand search insufficiently sensitive to identify all patients that presented with head injury in the 6 months time frame. What selection biases were present when the hand search was conducted are not known and were assumed to be randomly distributed. However, the parts of this project that depended on the head-injury data set identified in this manner are prone to any biases that led to some patients being more likely to be
identified by the hand search than others. The parts of the project dependent on
cohorts derived from the hand search were the overall estimate of head-injury
patients attending after twenty-four hours of injury and the primary reason these
patients had for ED attendance.

Hand searching identified 8.1% (95% C.I. 6.7%-9.6%) of patients as attending
after twenty-four hours of injury, but 15.5% (95% C.I. 12.7%-18.3%) of CT head
scans were found to be requested for patients presenting after twenty-four hours.
This may reflect the fact that patients presenting after twenty-four hours of injury
were disproportionately more likely to have a CT head scan, or that patients who
had a CT scan were more likely to be identified as presenting after twenty-four
hours of injury. CT head request data often included information about when the
injury had occurred, especially if the presentation after the injury was delayed.
The proportion of patients presenting after twenty-four hours identified
additionally through the CT head request system is higher (18.4% (95%C.I
14.4%-22.4%)) than that identified through hand searching alone (11.5%
(95%C.I. 7.9%-15.1%). The confidence intervals just overlap, but this is likely to
reflect systematic sampling bias and prevent direct comparison between the
groups identified by these different methods.

Discussion

This study is the first to estimate the proportion of head-injury patients that
present more than twenty-four hours following a head injury. The systematic
review component of this project could only identify an abstract that specifically
studied this group (Borczuk, 1997). The estimates are larger than envisioned with
only 6.9% of GCS 15 head-injury patients previously being identified as
presenting after twelve hours (2006, Hemphill et al., 1999). This current study
found that 8.1% all head-injury attendances and 15.5% of CT head scans
completed for adult head trauma were for head-injury patients presenting after
twenty-four hours of injury. The lower proportion of patients presenting after
twelve hours is reported in an older study and in a different health setting.
The rate of intra-cranial injury found in this study is comparable to the rate of CT abnormality identified in head-injury populations found in previous studies (Harnan et al., 2011, Stiell et al., 2001, Haydel et al., 2000). This appears to be unaffected by time of presentation.

The use and sensitivity of NICE guidelines appears to be reduced by a delay in presentation of greater than twenty-four hours. This finding must be interpreted with some caution as it may reflect the confounding effects of recall bias and the limitations of the analysis conducted. Nonetheless, it is potentially very important. The fact that significantly more CT head scans were requested in NICE negative patients, presenting after twenty-four hours, indicates that the guidelines are regarded by clinicians as being less effective in this group. If NICE guidelines had been applied strictly then 30% of intra-cranial findings, including a finding that required neurosurgery, would have been missed in patients presenting after twenty-four hours of injury. This confirms that NICE guidelines are less effective at risk assessing patients that present more than twenty-four hours following a head injury.

The presence of a headache or patients attending for a medical review, were identified as the two most common reasons patients presenting after twenty-four hours of injury had for attending the ED. The significance of an on-going headache following a head injury is not known. It could represent benign pathology, or it could be indicative of serious intra-cranial trauma. Further research is required to assess whether this should be included in NICE guidelines as it is in the Australian equivalent (New South Wales Government Ministry of Health, 2012). Equally, it is debatable whether NICE indications for CT that relate to the circumstances of an injury need to be applied to the cohort of asymptomatic patients that present after twenty-four hours.
Conclusion

This part of the study has identified patients presenting after twenty-four hours of injury as a significant clinical population that accounts for 15.5% of all CT head scans completed for adult head trauma. Significant injuries were identified in this cohort of patients at a rate comparable to those presenting within twenty-four hours of injury. Existing guidelines were demonstrated as not being as effective at identifying injury in this group of patients. Further research and a different approach to this group of head injury patients may be required.
Chapter 5: Synthesis of findings and the implications of the completed research

This chapter outlines the findings of this three-phase project. It summarises what is currently known about the management and risk profile of delayed presentation head injury patients within the context of current Emergency Department practice in the UK. It assesses the strengths and weaknesses of the research undertaken and what the findings add to current knowledge about this group. On the basis of this recommendations for future research are made and the implications for current clinical practice and health policy are assessed.

Current management of delayed presentation head injury in the U.K.

As outlined in Chapter 1 the management of head injury patients in the U.K. is based upon the NICE guidelines (NICE, 2014). These are used to risk stratify the large number of minor head injury patients that present to the ED into patients that require a CT head scan to exclude neurosurgical pathologies, and patients that are of sufficiently low risk to allow discharge with advice. The overall risk of such injuries in this group is low. Only 1% of such patients will require neurosurgical intervention and approximately 5% of patients will require hospital admission due to the injuries that they have sustained (Pandor et al., 2011). However such pathologies are life threatening and therefore their identification is imperative (Kim et al., 2013).

The NICE guidelines regarding the risk assessment of minor head injury patients and their triage for CT head scan are based on the CCHR (NICE, 2014). This was derived and validated in populations presenting within twenty-four hours of injury. The NICE guidelines are aimed primarily at informing the management of the first twenty-four hours following a head injury. However, patients do not necessarily present within twenty-four of sustaining a head injury. There is evidence that minor head injury patients with neurosurgical pathology will
deteriorate within the first twenty-four hours following a head injury (Choudhry et al., 2013, Reynolds et al., 2003). They may therefore be a lower risk sub-population. It has also been hypothesized that minor head injury patients presenting in a delayed manner may be a self-selecting high risk group due the persistence or worsening of symptoms (New South Wales Government Ministry of Health, 2012).

The context for this project was that well validated guidelines existed for the management of mild/minor head injury patients for patients presenting within twenty-four hours of injury. These guidelines had however not been tested in patients presenting after this. Moreover, there was some evidence that patients presenting after twenty-four hours may have a different risk profile. Therefore, the application of the NICE guidelines to this group potentially risks over investigation or failing to identify important injuries. This project aimed to systematically identify all existing research about this group. It also aimed to explore the current clinical management and risk profile of delayed presentation head injury patients through a clinical vignette based survey and analysis of audit data.

**Summary of key findings**

The systematic review component of this project found there to be few existing studies of poor methodological quality that assessed the incidence of injury and risk profile of delayed presentation head injury patients. Patients presenting after twenty-four hours of injury were found to be a significant clinical population. Analysis of the audit data found 8.1% (95% C.I. 6.7%–9.6%) of head injury attendances were for patients presenting more than twenty-four hours following their injury. Additionally, 15.5% (95% C.I. 12.7%–18.3%) of completed CT head scans for adult head trauma were for patients presenting after twenty-four hours of injury.
Despite evidence that the majority of minor head injury patients with neurosurgical pathology deteriorate within twenty-four hours of sustaining their injuries (Choudhry et al., 2013, Reynolds et al., 2003), a similar incidence of intra-cranial injury was found in adult patients that had undergone a CT head for head trauma that presented within, and after, twenty-four hours of injury. The rate of intra-cranial injury in patients presenting within twenty-four hours was 8.4% (95%C.I. 6.1%-10.7%), compared to 9.9% (95%C.I. 4.1%-15.7%) in patients presenting after twenty-four hours of injury. More significantly the rate of neurosurgical intervention was also comparable in these groups: 0.9% for patients presenting within twenty-four hours and 3.0% for patients presenting after.

Clinicians were also found to be less likely to apply the NICE guidelines when deciding whether to request a CT head scan in delayed presentation head injury patients. Analysis of the audit data shows that three times more CT head scans were completed for patients with no NICE indication when patients presented after twenty-four hours of injury. However, the responses to the clinical vignette show that in general clinicians are less likely to request a CT head scan despite the presence of a NICE indication as delay in presentation increases. Factors not present in the NICE guidelines and the length of delay in presentation seem to affect clinician decision making within this group.

Analysis of the audit data provides evidence that the NICE guidelines are less effective at predicting significant injuries in patients presenting after twenty-four hours of injury. The sensitivity of the NICE guidelines for intra-cranial injuries was 70% in patients presenting after twenty-four hours of injury compared to 97.8% for patients presenting within twenty-four hours of injury. Moreover, the risk of having an intra-cranial injury when no NICE indication was present was 1.3% for patients presenting within twenty-four hours of injury compared to 7.7% for patients presenting after twenty-four hours of injury. This indicates that the NICE guidelines are less effective at predicting significant injuries in patients presenting after twenty-four hours of injury.
Strengths and weaknesses of the completed research

The systematic review component of this project was methodically, transparently and reproducibly conducted and reported in line with PRISMA guidelines (Moher et al., 2010). The main weakness is small number of poor quality studies identified, which prevented meaningful conclusions about the risk-profile of delayed presentation head injury population. The time and resource constraints placed on the project limited the extent of the literature search to two electronic databases and the reference list of key head injury guidelines. Potentially, relevant studies may not have been identified. However, the most valid and important conclusion of the systematic review is that little research of poor quality has been conducted about delayed presentation head injury patients. The search strategy utilised is of sufficient strength to show this to be true.

In isolation, the results of the clinical vignette based survey must be interpreted with some caution. The low response rate of only 11% of the target population makes the results highly susceptible to non-responder bias. The way in which the survey was conducted also makes it susceptible to sampling biases. Finally, the internal validity of clinical vignettes in general is questioned, and the responses to the vignettes in this study may have been biased by order effects. Nonetheless, the responses consistently showed that increasing delay in presentation affects whether clinician apply NICE head injury guidelines to delayed presentation head injury patients and, that there is no clinical consensus regarding the management of this group. These findings are supported by the fact that three times more CT head scans were found to be completed for patients with no NICE indication who presented after twenty-four hours of injury, compared to those presenting within twenty-four hours of injury. The results of the clinical vignette based survey are best interpreted within the context of the results of the rest of the project. The most supported conclusion is that a degree of clinical uncertainty exists regarding the management of delayed presentation head injury patients and, this is within a context of little available evidence to aid the clinical assessment of this group.
The use of the electronic requesting system to identify all CT head requests for adult head trauma is an accurate method to identify these data. Therefore, conclusions based on these data are likely to be accurate. This includes an estimation of how many CT head scans were completed for patients presenting after twenty-four hours injury as well as the incidence of intra-cranial injury in patients presenting within and after twenty-four hours of injury. However, the estimation of the incidence of intra-cranial injury overestimates injury, as the analysis does not include patients that have not undergone CT head scan. The assessment of the relative performance of current NICE guidelines in patients presenting within and after twenty-four hours of injury is also based on this data collection method. The apparent poorer performance of the NICE guidelines in patients presenting after twenty-four hours of injury does not appear to be due to confounding factors or systematic differences between the two groups. However, the effect of recall bias on the clinical assessment of delayed presentation head injury patients is difficult to measure. Limiting the focus of analysis to patients that have undergone CT imaging also means that the specificity of the guidelines cannot be assessed. This part of the project provides some evidence that the NICE guidelines may not be as effective in risk stratifying patients presenting after 24 hours of injury.

The identification of head injury attendances through hand searching was found to be unreliable. This method identified only approximately 50% of attendances associated with CT head scans identified by using the electronic request system. Therefore, analysis based on data identified through hand-searching alone may be less reliable. This includes the estimate of the total proportion of head injury attendances for patients that sustained their injuries more than twenty-four hour previously. As discussed in chapter four, the calculated 8.1% is likely to represent an under-estimate of the true size of the delayed presentation head injury population. The assessment of the reasons patients presenting after twenty-four hours of injury had for attending the ED is also limited by the utilisation of a case-note review method. This can underestimate or distort the actual events within a consultation (Shah et al., 2007).
What this research adds

This project provides evidence that patients presenting after twenty-four hours of injury are a clinically important group that accounts for approximately 1/10 adult attendances following a head injury and 15.5% of completed CT head scans for adult head trauma. This is the first study to estimate the size of the population of head injury patients that present more than twenty-four hours following an injury. There are at least 700 000 attendances to EDs in England and Wales a year of adults following a head injury (NICE, 2014). This is therefore a large national population of patients. It is also a larger clinical population than previous thought. One of the reasons cited by the authors of the original CCHR study for limiting the inclusion criteria to patients presenting within twenty-four hours of injury was that patients presenting after this represented too small a population to be clinically significant (Stiell et al., 2001). This does not appear to be true.

Analysis of the audit data showed a comparable incidence of injury in samples of patients presenting within and after twenty-four hours of injury that underwent CT for the investigation of head injury. Some patients required neurosurgical intervention more than twenty-four hours after sustaining a head injury. This is, as far as I am aware, the first study to directly compare the incidence of intra-cranial injury between delayed presentation and non-delayed presentation head injury groups. The results show that despite evidence that minor head injury patients with neurosurgical pathologies deteriorate within twenty-four hours of sustaining their injuries (Choudhry et al., 2013) (Reynolds et al., 2003), patients presenting after twenty-four hours of injury are not a more benign sub-population.

This project has provided evidence that clinicians are less likely to use NICE guidelines when deciding which patients require a CT head scan in the delayed presentation head injury population. Clinicians are both more likely to request a CT head scan for non-NICE indications when head injury patients present more
than twenty-four hours after an injury, and not request a CT head scan when a NICE indication is present in this group. The clinical vignettes and analysis of the audit data represent the only attempts to my knowledge to assess whether clinicians apply the current NICE head injury guidelines to delayed presentation head injury patients. The results show that clinicians regard the NICE guidelines to be less effective at the risk assessment of this group and that no clear consensus exists regarding the management of delayed presentation head injury patients.

Analysis of the audit data showed that a significant minority of patients, approximately 25%, presenting after twenty-four hours of injury were asymptomatic. This is a group that clinicians may regard as not requiring CT imaging irrespective of the presence of NICE indications relating to the patients demographics and circumstances of injury. Neurosurgical pathology may not just manifest as clinical deterioration within the first twenty-four hours, but may also result from persistent symptoms. The asymptomatic period in this group may make them a lower risk sub-population of delayed presentation patients.

Due to the potentially catastrophic consequences of failing to identify injuries that require neurosurgical intervention, the NICE guidelines are intended to be highly sensitive and identify all neurosurgical pathologies (Pandor et al., 2011). In the sample of patients presenting after twenty-four hours of injury analysed the NICE guidelines were found to fail to meet this standard. If applied strictly, a patient that required a neurosurgical intervention would not have undergone an immediate CT head scan. This project has shown the NICE guidelines to be less effective at the risk-assessment of patients presenting after twenty-four hours of injury. The sensitivity of the guidelines was lower in this group. The presence of a NICE indication for a CT head scan was found not to be statistically predictive of significant intra-cranial injuries in patients presenting after twenty-four hours of injury. This research adds the clinically important finding that the absence of a NICE indication for a CT head scan does not rule out significant intra-cranial pathology in patients presenting more than twenty-four hours after a head injury.
Implications For Future Research

The most important future research question is to determine which factors predict significant intra-cranial injuries in patients presenting after twenty-four hours of injury. This project has identified patients presenting after twenty-four hours of injury as having a similar rate of intra-cranial pathology to non-delayed presentation patients, though different features may predict injury in this group. Factors present in the NICE guidelines that relate to the circumstances of injury such as the presence of a dangerous mechanism may not predict the presence of significant intra-cranial injuries in asymptomatic delayed presentation head injury patients. Approximately 25% of patients presenting after twenty-four hours of injury were found to be asymptomatic. Strict application of aspects of the NICE guidelines relating to the circumstances of an injury may risk over-investigation of this group. Conversely, 30% of intra-cranial injuries detected in patients presenting after twenty-four hours of injury were in patients with no NICE indication for a CT head scan. On-going symptoms not included in the NICE guidelines such as a headache or dizziness may predict injury in this group.

A decision-rule derivation study of minor head injury patients presenting after twenty-four hours of injury could be used to create a recursive partitioning model to test which NICE indications predict injury in patients presenting after twenty-four hours of injury. Additionally, whether the presence of specific on-going symptoms predict significant intra-cranial injury in this group could also be assessed. Using the formula \( N = \frac{10k}{p} \), where \( K \) is the number of covariates and \( P \) is the proportion of outcomes, then such a study would require 3000 participants to model 15 co-variants if the proportion of clinically significant intra-cranial injury is approximately 5% (Stoltzfus, 2011, Pandor et al., 2011). As delayed presentation head injury patients account for only 10% of all head injury attendances this would ideally be a multicentre study to optimise the chances of recruiting the requisite number of patients.
Implications for policy

The current NICE guidelines make no recommendations regarding the management of delayed presentation head injury patients (NICE, 2014). Based upon the findings of this research I believe these national guidelines should acknowledge that they may fail to effectively risk assess this group. Factors not present in the NICE guidelines such as on-going symptoms may predict significant injuries in this delayed presentation head injury patients and if clinicians mistakenly apply the NICE guidelines strictly to this group important injuries may not be detected. The NSW guidelines have a specific section regarding the management of delayed presentation head injury patients (New South Wales Government Ministry of Health, 2012). Recommendations for the management of this group are made on the basis that they may have a different risk profile to non-delayed presentation head injury patients and should be treated with caution. A low threshold for a CT head scan is recommended for patients with persistent symptoms. Until further research is conducted this appears to be a safe health policy recommendation and one that should be adopted in the U.K.

Implications for clinical practice

As an ED clinician, the most important finding of this research is that the absence of a NICE indication for a CT head scan does not effectively rule out significant intra-cranial injuries and neurosurgical pathology in patients presenting after twenty-four hours of injury. Until further research is conducted it is therefore justifiable to conduct CT head scans on delayed presentation head injury patients with persistent symptoms not accounted for by the NICE guidelines. The factors present in the NICE guidelines still predicted the majority of injuries in patients presenting after twenty-four hours of injury. Therefore a cautious clinical approach would be to also complete CT head scans on all patients with NICE indications. This is likely to over-investigate asymptomatic patients with NICE indications relating to the circumstances of the injury but until further research is conducted this represents the safest clinical practice.
Conclusion

Head injury patients presenting after twenty-four hours of injury represent a clinically important ED population. Existing research regarding this group is sparse and head injury clinical decision-rule research has focused on patients presenting within twenty-four hours of injury. This project demonstrated a significant degree of clinical variation in the application of existing NICE head injury guidelines to delayed presentation head injury patients. In addition to this, current NICE guidelines were shown to be less effective at identifying significant injuries in patients presenting after twenty-four hours of injury. A different approach to the current NICE guidelines is required in head injury patients presenting after twenty-four hours in order to identify significant injuries and avoid over investigation. Further research is required to identify the risk factors that predict significant injuries within this group. Until this research is conducted a cautious clinical approach should be taken to the management of delayed presentation head injury patients and this should be recommended in national guidelines.
List of References:


application in ICD-11 field studies. *International Journal of Clinical and Health Psychology*.


https://www.shef.ac.uk/scharr/sections/hsr/emris/ahead


The risk of a bleed after delayed head injury presentation to the ED: systematic review protocol.

Carl Marincowitz, Christopher M. Smith, William Townend
Emergency Department, Hull Royal, Hull, UK

Correspondence to:
Dr Carl Marincowitz, CT3 Emergency Medicine, Emergency Department, Anlaby Road, Hull, HU3 2JZ

Registered with PROSPERO 2015:CRD42015016135 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015016135

The protocol was designed in accordance with PRSIMA guidelines [1].

Contributors:
CM had the idea for the systematic review. CM and CSM developed the protocol, and will undertake the electronic search, data extraction, quality assessment and data synthesis. WT has a supervisory role.

Support:
CM is an academic clinical fellow in emergency medicine and therefore indirectly receives funding from the National Institute of Health Research. There are no other sources of support or funding for this systematic review.

**Introduction**

Head injuries represent a very common reason for attendance to Emergency Departments (ED) – in England and Wales an estimated 1.4 million such attendances occur a year[2]. Ninety-five percent of these attendances are patients with minor/mild head injuries, as defined by a Glasgow Coma Scale (GCS) score of 13, 14 or 15 [2] [3]. Research has been directed at differentiation of patients with minor/mild head injury into those who are sufficiently low risk to be discharged on the basis of clinical history and examination alone and those who require a Computed Tomography (CT) scan of the head to rule out serious intra-cranial pathology. In the UK, National Institute for Health and Clinical Excellence (NICE) guidelines are used to facilitate this risk assessment, which are based upon the Canadian CT head rules (CCHR) [4]. The CCHR was derived in a population of patients presenting within 24 hours. Both the NICE guidelines and CCHR have only been validated in populations of patients presenting within 24 hours [2] [5-10].

Not all patients present to the ED immediately after sustaining a head injury with some presenting after 24 hours [11]. There is some evidence that patients with a minor head injury and intra-cranial haemorrhage will deteriorate within 24 hours [12][13]. Therefore, patients who present after 24 hours may be a distinct and more benign sub-population. Application of current guidelines may risk over-investigating this group.

However, there are case reports of patients with delayed onset intra-cranial haemorrhage following a head injury [14] [15]. This pathology can occur many
days after the initial injury as can clinical deterioration. Also, patients who re-present to the ED after a head injury are an established high risk group [16].

Time of presentation to the ED following a head injury could affect the likelihood of intra-cranial pathology. This has implications to the risk assessment of patients who present in a delayed manner, especially as guidelines which aid this have only been validated in patients that present within 24 hours.

This systematic review aims to assess whether delay in presentation following a head injury affects the likelihood of intra-cranial pathology. The relevant population is patients presenting the ED following a head injury. The intervention is delay in presentation. The comparator is of patients presenting acutely. Outcome measures are of traumatic findings on CT scan, death and neurosurgery.

**Methods:**

Eligibility:

The nature of this systematic review question precludes the inclusion of RCTs and therefore lower level evidence will be evaluated. Preliminary review of the literature also indicates that there are likely to be few studies of poor quality. Therefore the following inclusion and exclusion criteria will be applied. Studies must be conducted in populations of patients presenting in a delayed manner to the ED following a head injury. No specific time as to what constitutes a delay will be applied but included studies must specifically evaluate a population of patients who have presented after a defined time delay. Included studies must measure an outcome of traumatic intra-cranial pathology as identified by CT scan. Any study design, apart from single cases studies, will be included.

Information Sources:
NICE [1], SIGN [17] and NSW [18] head injury guidelines and bibliographies will be reviewed for any relevant studies. MEDLINE and EMBASE will be searched with the electronic search strategy present in the appendix. Bibliography searches of articles identified through the electronic search strategy will also be undertaken.

Data handling and extraction:

Electronic searches will be saved on OVID online and transferred to the electronic storage facility of endnote. Studies identified by additional sources will be uploaded to end note. Studies will be considered for inclusion through a title and abstract review of papers identified from the electronic searches and by review of bibliographies by two independent reviewers (CM and CMS). Potential papers will be assessed against the pre-defined inclusion criteria. The full-texts of potentially relevant studies will be obtained and reviewed for final inclusion. Disagreement will be resolved by discussion or referral to WT. Data extraction will include the nature of the population being studied, notably the time of delay in presentation, type of study, outcome measures and results. The primary outcome being assessed is any traumatic intra-cranial pathology as identified by CT. Secondary outcomes of death and need for neurosurgery will also be extracted. As the types of studies included may vary a descriptive quality assessment, including for risks of bias, will be undertaken at the data extraction stage. As cohort studies are anticipated to be identified this quality assessment will be informed by the Ottawa-Newcastle Scale [19].

Data Synthesis and Meta-analysis:

As few studies of variable methodology and quality are anticipated to be identified only a narrative data synthesis is planned. Meta-analysis of studies identified is also thought not to be possible and therefore is also not planned.
References:


Appendix 2: Electronic Search Strategy

Embase search undertaken 23/1/2015 and Medline search undertaken 29/1/2015

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<td>2246</td>
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<td>8. (head injur* or brain injur*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]</td>
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Appendix 3: Letter from Research and Ethics Committee

NRES Committee Yorkshire & The Humber - Leeds West
Room 001, Jarrow Business Centre
Rolling Mill Road
Jarrow
Tyne and Wear
NE32 3DT

Telephone: 0191 428 3387

19 December 2014 (Reissue)

Dr Carl Marinowitz
1a Riverstreet
York
YO23 1AT

Dear Dr Marinowitz,

Full title of study: Does delay in presentation of greater than 24 hours in minor head injury reduce the likelihood of intra-cranial pathology?

REC reference number: 15/YH/0008
IRAS project ID: 168350

Thank you for responding to my emails and speaking to me regarding your application. I can confirm that following these discussions the above application for ethical review has been withdrawn for the following reason:

- The application does not require NHS REC review under the Governance Arrangements for Research Ethics Committees. The research is limited to the secondary use of information previously collected in the course of normal care (without an intention to use it for research at the time of collection), and the patients or service users are not identifiable to the research team in carrying out the research. The identifiable data will be collected by the clinical care team and anonymised for the purposes of the research for the research team. Confirmation of this is available on the HRA website at http://www.hra.nhs.uk/resources/research-legislation-and-governance/governance-arrangements-for-research-ethics-committees/ and http://www.hra.nhs.uk/resources/before-you-apply/is-nhs-rec-review-required/

Please feel free to use this letter as proof that NHS REC review is not required.

I wish you the best of luck with your research.

15/YH/0008 Please quote this number on all correspondence

Yours sincerely

Sarah Grimshaw
REC Manager

Email: nrescommittee.yorkandhumber-leedswest@nhs.net

A Research Ethics Committee established by the Health Research Authority
### Appendix 4: Specific intra-cranial injuries identified

<table>
<thead>
<tr>
<th>Traumatic Abnormalities</th>
<th>Number</th>
<th>Percentage of total injuries</th>
<th>Within 24 hours (%total injuries in brackets)</th>
<th>After 24 hours (%total injuries in brackets)</th>
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<tr>
<td>Extra-dural</td>
<td>6</td>
<td>10.7%</td>
<td>5 (10.9%)</td>
<td>1 (10.0%)</td>
</tr>
<tr>
<td>Sub-dural</td>
<td>14</td>
<td>25.0%</td>
<td>8 (17.4%)</td>
<td>6 (60.0%)</td>
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<tr>
<td>Sub-arachnoid</td>
<td>9</td>
<td>16.1%</td>
<td>8 (17.4%)</td>
<td>1 (10.0%)</td>
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<td>Skull Fracture</td>
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<td>14.3%</td>
<td>7 (15.2%)</td>
<td>1 (10.0%)</td>
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<td>Contusion</td>
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<td>7.1%</td>
<td>4 (8.7%)</td>
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<tr>
<td>Intra-cerebral Haemorrhage</td>
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<td>10.7%</td>
<td>6 (13.0%)</td>
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</tr>
<tr>
<td>Skull Fracture+ Contusion</td>
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<td>5.4%</td>
<td>2 (4.3%)</td>
<td>1 (10.0%)</td>
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<tr>
<td>Skull Fracture+ intra-cerebral haemorrhage</td>
<td>6</td>
<td>10.7%</td>
<td>6 (13.0%)</td>
<td>0</td>
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