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https://doi.org/10.1089/neu.2017.5259

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The risk of deterioration in GCS13-15 patients with traumatic brain injury identified by CT imaging. A systematic review and meta-analysis.

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<td>NEU-2017-5259.R1</td>
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<td>Manuscript Type</td>
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<td>Date Submitted by the Author:</td>
<td>02-Nov-2017</td>
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<td>Complete List of Authors:</td>
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<tr>
<td>Keywords:</td>
<td>ADULT BRAIN INJURY, HEAD TRAUMA, TRAUMATIC BRAIN INJURY, CT SCANNING</td>
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<tr>
<td>Manuscript Keywords (Search Terms):</td>
<td>Mild Traumatic Brain Injury, Prognostic modelling, Intra-cranial haemorrhage, Minor Head Injury</td>
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Dear Editor of The Journal of Neurotrauma,

Thank you for considering our manuscript and the time that Reviewer 1 has taken to review our manuscript and their useful comments. Our response to their individual points follows below.

Most studies of “mild TBI” currently do not refer to GCS because these truly mild cases almost always have a GCS of 15. Thus, GCS is eliminated as a measure of concussion or the severity of concussion. “Mild TBI” is an undesirable term because we do not know if the authors are referring to the whole range of patients with mild TBI which includes GCS of 13, 14 or 15. For this reason, MTBI is becoming an outmoded term because it encompasses a heterogeneous population ranging from those with focal neurological deficits which are clearly not “mild” and certainly not concussions, and those with no focal brain injuries which are concussions. Currently, the term concussion is preferred for brain injured patients with no focal neurological deficits who are almost always GCS 15. The admixture of GCS 13 and 14 makes this a very heterogeneous group. Since cases with GCS 13, 14 or 15 are a heterogeneous group, the data must be looked at separately, as the authors have done in some of their analyses. Those with and without a normal GCS, in other words cases with GCS 13 and 14, should be analysed separately from GCS 15 cases. This paper provides proof that mild TBI is a heterogeneous mixture and should be avoided. They have done this for GCS from 14 to 15, in some of the figures, but why did they exclude GCS of 13? Studies without sufficient data to allow analysis of the effect of GCS should have been excluded.

We agree that the terminology used to categorise traumatic brain injury can be used inconsistently in the literature and in clinical practice. We agree that mild TBI refers to a spectrum of traumatically induced brain dysfunction in GCS 13-15 patients, of which only a subset will have injuries identified by CT imaging. We have used the term “mild TBI” to refer to patients with brain injury who present to the Emergency Department with an initial GCS 13-15. This is consistent with the definition of mild TBI described in the Reviewer’s comments. We tried to make clear that our study population of interest is GCS 13-15 patients, who are therefore defined as having mild TBI, with injuries identified by CT imaging. This is outlined in the first 3 lines of page 5. We believe the description of our population of interest as patients with “mild TBI” with injuries identified by CT imaging best defines the group in the absence of a better alternative. We have changed the title, paragraph 6 of the background and paragraph 3 of the section entitled context to try to further clarify that our study population of interest is mTBI patients with injuries identified by CT imaging.

We agree that this population is a heterogeneous group with a range of characteristics that mean individual risk for adverse outcomes varies. Our findings suggest that despite being able to identify individual factors that affect risk in this group there currently is no risk model that using these or other factors can reliably identify low-risk patients. Initial GCS certainly represents one important factor that affects the risk of adverse outcomes in this group. We feel stratifying analysis by initial GCS would potentially lose important
information regarding how GCS and other risk factors interact, especially as older patients present with a higher GCS relative to the severity of their injury. We have added to paragraph 3 of the summary section of the discussion to highlight this point. Moreover, the vast majority of the studies that we identified did not stratify their analysis by the initial GCS of the study population and studies that attempted to derive prognostic models included GCS as a prognostic factor. Therefore, it is not possible to assess either outcomes or risk factor effect with only studies that would allow the separate analysis of different initial GCS populations without losing the majority of the study data we have identified. We have assessed the effect that an initial GCS of 15 has on the risk of adverse outcome using both stratification of outcomes by study GCS inclusion criteria (Fig 2 and Fig 5), meta-regression (Fig 4 and Fig 6) and pooling of within study estimates of the effect GCS (supplementary material 6). Figure 2 and Figure 5 include stratification of outcome prevalence by initial GCS 13-15, GCS 14-15 and 15 using study inclusion criteria.

Indeed the abstract indicates that after all their analysis they are saying that the only factors that indicate later deterioration are those with low initial GCS, advancing age and anticoagulation medication. Most clinicians in the field already know this. Then they conclude that research is needed to determine a usable clinical decision rule. In other words as a result of their study they found that there is no useful rule. It is not clear why they did not state a rule that patients with low GCS, advanced age or anticoagulation cannot be discharged from the ED and should be admitted for observation. Wasn’t that the purpose of their study?-

We believe that what our study shows is that despite there being a large number of studies that have estimated the risk of adverse outcomes in the population of interest and some studies that have attempted to identify the factors that affect risk in this group, we cannot currently identify individual low risk patients that do not require hospital admission. Until a clinically useable validated multivariable prognostic model with sufficient sensitivity and specificity can accurately identify low-risk patients we believe that the risk of significant adverse outcomes in this group is sufficiently high that all patients in this group should be routinely admitted for observation. This position is outlined in the first 5 lines of page 21.

The exclusions are not clear. For example, did they exclude studies of patients who did not go through ED, and went directly to a hospital ward? Did they exclude patients who went to facilities not connected with a hospital. There was massive exclusion of studies. Case studies were automatically excluded. Why? There was one cohort study included. Why? To the authors are case and cohort studies synonymous? If so, then they should be consistent. They were critical of studies with “bias” and those not seen in emergency departments. Why? Why would head injured patients admitted directly to neurology, neurosurgery or anywhere else be considered a biased sample? Why are those seen in family doctors offices “biased”, or remote nursing stations “biased”?

Mary Ann Liebert, Inc, 140 Huguenot Street, New Rochelle, NY 10801
We agree that the explanation of the study exclusion criteria regarding the study setting could be clearer. The section in inclusion criteria entitled participants has now been amended to make it clear that only study participants who attended the ED or were admitted to an inpatient ward were included. The reason we have only included this population is because the study was aimed at informing clinicians evaluating patients in the ED about the potential risk of adverse outcomes in the GCS13-15 patients with brain injuries identified by CT imaging. Patients presenting in a different clinical setting to this may have a different risk profile and therefore conclusions drawn from them may be less applicable to the ED setting.

We feel that the nature of a systematic review means that study exclusion is determined by transparent and a prior defined criteria and that a large number of excluded studies may reflect a sensitive and well conducted search strategy. Our number of studies excluded following title and abstract screening and review of full studies is comparable to that of other systematic reviews including a previous systematic review of prognostic models in TBI that included 53 studies from 3354 studies identified by their search strategy.1

Case studies were excluded as it would not be possible to estimate the study prevalence of the adverse outcomes of interest from single case studies or small case series. As indicated in supplementary material 4 all the studies included were cohort studies apart from a single small prospective trial.

The purpose of this study was to identify risk factors which could help clinicians decide whether a patient being evaluated in the ED requires a hospital admission. Therefore, if the patient population was drawn from a context in which patients were likely to have higher acuity injuries, such as patients selected for repeat CT imaging, then outcome estimates may not be as applicable. We agree that bias is not the correct term to describe the effect that different population selection has on outcome measures. The final sentence of the 4th paragraph of the abstract has been changed to reflect this. We do not believe that the use of bias in the rest of the main text refers to study population selection.

What % of cases had MR imaging, and why were they not analysed using normal vs abnormal MRI?

We intended that this study would help clinicians risk stratify patients using the initial CT scan and other patient factors available at presentation. Existing national guidelines including the UK NICE and SIGN guidelines, the Australian New South Wales Guidelines and the Canadian CT Head rule recommend initial CT imaging of head injured patients. We agree that MRI imaging may provide additional useful prognostic information but this may not be available to a clinician in the ED making a decision about whether patients in this group require hospital admission.

It is not clear why some of the focal lesions, especially extradural hematomas fail to make the list of reliable risk factors.
We agree that our study indicates the type of focal lesion identified by CT imaging is an important risk factor for deterioration in this group. The 4th paragraph of the abstract and discussion summary section has been amended to highlight the importance the type of focal lesion has on the risk of the adverse outcomes of interest.

*I am not sure why IMPACT was mentioned. It would be a completely inappropriate test for this group of patients.*

IMPACT and other prognostic models derived in patients with more severe TBI were mentioned to illustrate that it has been possible to develop clinically useful prognostic models for the heterogeneous group of patients with more severe TBI. The 4th paragraph of the background has been amended to make it more explicit that these cannot be applied to the population of interest in this study.

*The paper needs some editing for grammar and missing words including the abstract which contains a sentence without a verb.*

Paragraph 3 and 4 of the abstract, the section entitled search methods for study identification, paragraph 2 of the section entitled quality assessment and paragraph 4 and 5 of the background have been amended.

*For those unfamiliar with the methodology, terms should be more carefully described such as studies “were retrieved”. What does this mean in plain language? Jargon such as this should be minimised to improve reader understanding.*

We have replaced the term retrieved with selected in the paragraph entitled study selection to improve reader understanding.

*The following sentence requires an explanation by the authors: “Factors potentially affecting the risk of adverse outcomes were considered if there were patient characteristics present at admission or available from initial investigations”. There are multiple issues that they may have arbitrarily decided to exclude such as drug overdose, alcoholism, diabetes, etc.*

This sentence has been amended to make it clear that any factor included in any of the studies providing it was present at admission was included in analysis. This would include drug overdose, alcoholism and diabetes.

*“Neurosurgery” as an outcome measure is probably a poor term. Most clinicians regard “neurosurgery as a profession rather than an outcome measure. The performance of a neurosurgical procedure or the requirement for a neurosurgical operation would be better.*
We have replaced the term neurosurgery with neurosurgical intervention throughout.

We hope that we have adequately addressed the feedback and that the paper is now ready to be considered for publication.

Yours sincerely,

Carl Marincowitz

The risk of deterioration in CT-identified GCS13-15 patients with traumatic brain injury identified by CT imaging. A systematic review and meta-analysis.

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Abstract

The optimal management of mild traumatic brain injury (TBI) patients with injuries identified by CT brain scan is unclear. Some guidelines recommend hospital admission for an observation period of at least 24 hours. Others argue that selected lower-risk patients can be discharged from the Emergency Department (ED).

The objective was to estimate the risk of death, neurosurgical intervention and clinical deterioration in mild TBI patients with injuries identified by CT brain scan, and assess which patient factors affect the risk of these outcomes.

A systematic review and meta-analysis adhering to PRISMA standards of protocol and reporting. Study selection was performed by 2 independent reviewers. Meta-analysis using a random effects model was undertaken to estimate pooled risks of: clinical deterioration, neurosurgical intervention and death. Meta-regression was used to explore between-study variation in outcome estimates using study population characteristics.

Forty-nine primary studies and 5 reviews were identified that met the inclusion criteria. The estimated pooled risk of the outcomes of interest were: clinical deterioration 11.7% (95% CI: 11.7 to 15.8); neurosurgical intervention 3.5% (95% CI: 2.2 to 4.9%); death 1.4% (95% CI: 0.8% to 2.2%).

Twenty-one studies presented within-study estimates of the effect of patient factors. Meta-regression of study characteristics and pooling of within-study estimates of risk factor effect found the following factors significantly affected the risk of adverse outcomes: age; initial GCS; type of injury and anti-coagulation. The generalisability of many studies was limited significantly susceptible to bias due to population selection.
Mild TBI patients with injuries identified by CT brain scan have a small but clinically important risk of serious adverse outcomes. This review has identified several prognostic factors. Research is needed to derive and validate a usable clinical decision rule so that low-risk patients can be safely discharged from the ED.

Keywords: Mild Traumatic Brain Injury; Prognostic modelling; Intra-cranial haemorrhage; Minor Head Injury.
Background

There are 1.4 million annual attendances in England and Wales to Emergency Departments (EDs) following a head injury (any trauma to the head), and in 2010 2.5 million people were treated for traumatic brain injury (TBI- injury to the brain or alteration of brain function due to an external force) in the United States.\(^1\) Approximately 95\% of patients have an initial Glasgow Coma Scale (GCS) of 13-15, out of a possible 15, indicating normal or mildly impaired responsiveness and orientation.\(^2\)

In this large group with head injury and a high conscious level at presentation research has focused on developing decision rules to identify patients who require computed tomography (CT) imaging due to their risk of life threatening traumatic brain injury (TBI).

In the United Kingdom (UK), National Institute for Health and Care Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) guidelines are used for this risk assessment, based on the Canadian CT head Rule (CCHR).\(^1,3,4\) Only 1\% of head injured patients have life threatening TBI.\(^1,4\)

However, 7\% have TBI identified by CT imaging.\(^5\)

Most TBI patients who require neurosurgical intervention are identified soon after presentation. The optimal management of the remaining patients in this group remains controversial. A proportion will deteriorate due to the progression of their injuries and so some studies advocate admission to higher dependency levels of care and repeat CT imaging.\(^6,7\)

Others\(^8,9\) studies report that some low risk patients may be safely discharged after a short period of observation in the ED.\(^8,9\) Perel et al have previously outlined how prognostic models can aid clinical decision making in TBI.\(^10\) Subsequent prognostic models, including the IMPACT, TARN and CRASH models,\(^1,10\) have been useful in predicting adverse outcomes in patients with more severe TBI, but they are not applicable to this patient group due to the exclusion of GCS15 patients.\(^11-13\) Equivalent prognostic models for GCS13-15 patients with CT identified TBI may help safely reduce hospital admissions.
This review is the first to give an overview of the risk of adverse outcomes and prognostic factors in patients with mild TBI (that is, a high or normal conscious level with traumatically induced brain dysfunction) and injuries identified by CT brain scan and injuries identified by CT brain scan have of adverse outcomes and which patient factors are prognostic. The review specifically:

(i) Estimates the overall risk of adverse outcomes in patients who are initially GCS13-15 in the ED when traumatic brain injury is identified by CT imaging.
(ii) Assesses which prognostic factors affect the risk of deterioration and other clinically important outcomes in this population.

Methods

A systematic review was conducted using the PRISMA P protocol and is reported in accordance with PRISMA guidelines. The review is registered with the PROSPERO prospective register of systematic reviews and the protocol is available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016051585.

Inclusion Criteria:

Participants

Patients aged ≥12 years with an initial GCS of 13-15 with TBI identified by CT imaging. TBI included any traumatic: extradural haemorrhage, subdural haemorrhage, intra-cerebral haemorrhage, subarachnoid haemorrhage, cerebral contusion, or skull fracture. Studies had to be conducted in the context of an emergency hospital attendance including a presentation to the ED or during admission to an inpatient ward.

Prognostic factors

Factors potentially affecting the risk of adverse outcomes were considered if they were included in analysis if they were patient factors present at admission including: demographic characteristics,
comorbidities, medication use, symptoms, other clinical features patient characteristics present at admission or available from initial investigations.

Outcome measures

Primary outcomes: death, neurosurgical intervention or any other measure of clinical deterioration such that admission to hospital was warranted.

Secondary outcome: progression of TBI on repeat CT imaging.

Types of study design

All studies, other than case studies, were included.

Search methods for study identification:

Studies published before 1996 were excluded due to more liberal use of CT imaging to diagnose TBI after this date. The following electronic databases were searched with results restricted to English language studies:

- EMBASE (via OVID) searched 24/11/2016 1996 to 2016 Week 47
- MEDLINE (R) (via OVID) searched 24/11/2016 1996 to November Week 3 2016
- CINHAL plus (via EBSCO) searched 24/11/2016 1983 to 2016
- Cochrane Central Register of Controlled Trials (CENTRAL); The Cochrane Library 2016 all available dates. Accessed 24/11/2016

The full search strategy is reported in supplementary material 1.

The reference and citation searches of several national guidelines, reports and reviews included: NICE, SIGN and Australian New South Wales (NSW) guidelines, National Institute for Health Research (NIHR) Health Technology Assessment of management strategies for minor head injury, the results of the World Health Organisation (WHO) Collaboration on prognosis in mild traumatic brain injury, systematic reviews assessing prognostic factors in traumatic brain injury, and systematic reviews
assessing the utility of repeat CT imaging in minor head injury. All included studies references and citations were searched.

The Trauma Audit and Research Network (TARN) listed publications were searched via the TARN website: https://www.tarn.ac.uk/Content.aspx?ca=9&c=70 (accessed 10/3/2017).

Data Management and Extraction:

Identified studies were stored in EndNote X8 and duplicates removed.

Study Selection

Two reviewers (CM and AB) independently completed title and abstract screening. Full reports of any studies that potentially met the inclusion were selected and assessed retrieved. These were screened and studies that did not meet the inclusion criteria were discarded with documented reasons. Disagreements were resolved through discussion or arbitration by a 3rd reviewer (TS).

Data Extraction

The following data were extracted using a pre-piloted data extraction tool: study population and demographics, sample size, outcomes assessed, prognostic factors assessed, whether univariable or multivariable modelling had been undertaken and the overall results of the study. The selection criteria of studies were recorded to assess whether sub-populations with different risk profiles had been studied. The data extracted is presented in supplementary material 2.

Assessment of the risk of bias

The Quality in Prognostic Studies (QUIPS) Tool was used to assess the quality of included studies particularly for the risk of bias. Six domains were assessed: study participation; study attrition; prognostic factor measurement; outcome measurement; study confounding; and statistical analysis and reporting.
Data Analysis

Three forms of analysis were undertaken: pooling of adverse outcomes reported in studies, identification of risk factors by exploration of between-study variation in outcomes by study characteristics and a synthesis of common risk factors assessed within studies.

A pooled prevalence of the adverse outcomes of interest and confidence intervals for individual studies were estimated using the Metaprop function (STATA-SE 14). The Freeman-Tukey double arcsine transformation was used to include studies with no adverse outcomes and a random effects model was used due to study heterogeneity.

Between-study heterogeneity estimates of outcomes was explored using subgroup analysis. Meta-regression of study characteristics was used to identify factors that affected the risk of the outcomes of interest. Meta-regression of multiple study characteristics’ effect on the prevalence of adverse outcomes was assessed using the Metareg function (STATA-SE 14) with weighting incorporating a measure of between study variation (tau2). The log odds of clinical deterioration, and death were assessed as dependent variables and the standard error of the log odds was used to approximate the within study standard error. To account for studies with no outcomes, 0.5 was added to both the outcome estimates and the sample size (consequently, in graphic representations of the meta-regression the estimated risk can only tend towards zero).

Where studies had assessed the effect of risk factors on the outcomes of interest using individual data, analysis was categorised as univariable or multivariable. Univariable meta-analysis of prognostic factor effect estimates reported in primary studies was completed using Review Manager 5.3 where possible. A Random Effects model was used due to the heterogeneity of study populations, prognostic factor and outcome measures. Meta-analysis of multivariable models was not possible due to limited numbers and variation in outcome and prognostic factor measurement.
Results

Search Result

The electronic search strategy was completed on the 24/11/2016 and identified 4665 studies. Of these 412 were duplicates, leaving 4253 studies for title and abstract screening (Fig. 1). Following title and abstract screening 69 studies and 2 reviews were retrieved. A “grey” literature search identified a further 129 studies for title and abstract screening of which 3 were retrieved.

Reference and citation searching of included studies and selected reviews and guidelines identified another 46 studies for full retrieval and 3 additional systematic reviews for reference and citation searches.

In total 118 primary studies and 5 systematic reviews were retrieved.

Study Selection

Forty-nine primary studies met the inclusion criteria. Eight reviews presented new study data. The 4 remaining reviews formed part of the narrative synthesis. The reasons for excluding the remaining 69 studies are presented in supplementary material 3. Anonymised individual patient data were provided by the authors of a cohort study to allow outcomes for initial GCS13-15 patients to be calculated, so this study is included.

Study Characteristics

Supplementary material 4 presents the characteristics of included studies. Seven prospective studies were identified and 4 studies had a sample size of over 1000. Forty-six studies estimated the outcomes of interest and contribute to pooled estimates of risk. Four studies present data regarding specific injury sub-types. One study only contributes to the narrative synthesis.
due to the outcome measure it assessed. Three studies present the Brain Injury Guidelines (BIG) risk stratification tool. As this tool was applied to all TBI patients and initial GCS forms part of risk stratification, these studies contributed to the narrative synthesis.

Twenty-one studies present either univariate or multivariable analysis assessing prognostic factors’ effect on the outcomes of interest. Sixteen studies present multivariable models using logistic regression or recursive partitioning. Only 2 studies attempted to validate such models by splitting the study data sets.

Quality Assessment

QUIPS quality scores are presented in supplementary material 2. The following common methodological issues were identified.

Study recruitment was not representative of all GCS 13-15 patients with TBI identified by CT imaging. Sixteen studies that contribute to the pooled estimates of adverse outcomes only included patients that had undergone repeat CT imaging and so are likely to represent a higher risk population. Even when re-imaging was presented as routine practice, it was often indicated that not all patients were re-imaged and included in analysis. Many other studies excluded higher risk anti-coagulated patients or those with more severe injuries.

Prognostic factor measurement was not consistent. Continuous variables were dichotomised at different thresholds or the same risk factor was measured with different methods. For example, the severity of injury identified by CT imaging was assessed with 10 different measures. Most studies were retrospective and reliant on the accuracy of case notes and radiological reports. The small sample size of many studies prevented multivariable modelling with all variables identified in univariable modelling as affecting deterioration.
In 32 studies outcomes were assessed during inpatient admission and so patients who were discharged and deteriorated were missed. In other studies, it wasn’t clear when outcome measures were assessed. Eight different measures of clinical deterioration were used in 18 studies.

Several studies included patients with extra-cranial injuries and significant comorbidities. Extra-cranial injuries caused clinical interventions, and in studies that measured deterioration in this way this was a potential source of bias. Other studies indicated some recorded deaths were related to comorbidities instead of TBI.

### Risk of Adverse Outcomes and Exploration of Between-Study Variation

#### Death

Twenty-seven studies assessed the outcome of death. The estimated risk of death for these studies ranged between 0 and 6% (median 1.1%), and with a pooled prevalence of 1.4% (95% CI: 0.8% to 2.2%) (Fig. 2). Studies that selected only initial GCS15 patients had a pooled estimate of mortality of 0.03% (95% CI: 0 to 0.28%). Studies that selected populations for non-ICU admission or other conservative care pathways had an estimated prevalence of death of 0.1% (95% CI: 0 to 0.6%).

The effect on mortality of mean GCS, average age and selection of study population for a lower level of care was explored using meta-regression. Increased age of study population was associated with a higher risk of death (1.05 95% CI: 1.00 to 1.12) (Fig. 3). Whilst higher study population GCS was associated with a lower risk of death (0.12 95% CI: 0.02-0.86) (Fig. 4). The percentage of patients taking anticoagulants in studies was not associated with the prevalence of death (1.05 95% CI: 0.95-1.17), but selection for a lower level of care compared to a higher level of care was (0.27 95% CI: 0.08-0.94). When average age of the study population and mean study GCS were assessed in a multivariable model they remained statistically significant predictors of mortality (Table 1), with an
adjusted R squared of 38%, indicating that these 2 factors explained over a third of the variation in study estimates.

**Neurosurgery/Neurosurgical Intervention**

Thirty-six studies reported neurosurgical outcomes. Figure 5 presents the estimates of the proportion of patients that underwent a neurosurgical procedure stratified by the GCS inclusion criteria. Reported neurosurgical intervention prevalence ranged between 0 and 26% (median 3.1%). The high proportion requiring neurosurgical intervention reported by Beynon et al may reflect the greater use of anticoagulants or anti-platelets (33/70 participants).

The pooled estimated neurosurgical intervention risk was 3.5% (95% CI: 2.2 to 4.9%). An $I^2$ of 96.4% indicated considerable heterogeneity. Studies conducted on initial GCS 15 patients had a lower prevalence of neurosurgical intervention: 0.2% (95% CI: 0 to 0.5%). Sensitivity analysis of selection of the study population for reduced care, such as discharge, a non-ICU admission or non-routine repeat CT imaging found the pooled estimate of neurosurgical intervention in these studies to be 0.1% (95% CI: 0 to 0.5%).

The of result of meta-regression using: mean study population GCS, mean study population age, anticoagulation and selection of study population for non-ICU admission or other reduced care pathways is shown in Figures 6,7,8 and Table 1. Increasing age (1.01 95% CI: 1.02 to 1.11) and increasing percentage of study population taking anti-coagulants (1.1 95% CI: 1.01 to 1.19) was associated with a higher risk, whilst an increasing GCS (0.71 95% CI:0.01 to 0.56) was associated with a lower risk, of neurosurgical intervention.

Fig. 7 shows a cluster of 4 small studies with low mean ages that appear to have a disproportionately low estimated prevalence of neurosurgical intervention. This is explained by:
exclusion of anti-coagulated patients, selection of patients for non-ICU admission or other reduced care pathways, and exclusion of patients with large injuries.

When the effect of population selection for reduced clinical management, exclusion of anticoagulated patients (only 23/36 studies reported percentage of anti-coagulated patients), mean age and GCS of the study population were all included in a meta regression, age and GCS were the only statistically significant predictors of neurosurgical intervention (Table 1). The adjusted R squared of the model was 48%, indicating that these factors accounted for almost half of between study variation.

Clinical Deterioration

Eighteen studies measured prevalence of clinical deterioration. The estimated risk of deterioration ranged between 0 and 24.5% (median 12.8%). Figure 9 presents study estimates of the percentage of patients that deteriorated, with 95% confidence intervals and stratified by how the outcome was assessed. A pooled prevalence of 11.7% (95% CI: 8.21 to 5.8%) for some form of clinical deterioration was estimated with an $I^2$ of 95.7%.

Estimates were stratified by: initial GCS of patients, whether the included population were all selected for repeat CT imaging, the inclusion of anticoagulated patients, the follow up period and exclusion of patients with extra-cranial injuries. None of these factors reduced the observed between study heterogeneity.

The effect of: mean GCS study population, mean age study population, study population selection, exclusion of patients with extracranial injuries, and exclusion of anti-coagulated patients was explored using meta-regression. As only 18 studies measured this outcome the model was restricted to 2 variables. No factor assessed individually or in conjunction with another factor was found to statistically affect the risk of clinical deterioration. Higher age and lower GCS were non-statistically associated with a higher risk of clinical deterioration (Table 1).
Progression Repeat CT imaging:

Twenty-six studies assessed the outcome progression of the initial injury on repeat CT imaging. The prevalence of this outcome in these studies is presented in Figure 10, stratified by whether studies only included patients that had undergone repeat CT imaging. The pooled estimate for this outcome was 15.6% (95% CI: 11.3 to 20.4%). There is a high degree of heterogeneity with a range in risk of progression between 2% and 48% (median 36.5%) and $I^2=97\%$. The non-statistically significant higher pooled risk in studies that included only patients that had undergone repeat CT imaging probably reflects selection of higher risk patients to repeat imaging. Subgroup analysis of study characteristics did not find any factors that accounted for the heterogeneity. This is probably the result of different criteria used to triage patients to repeat CT imaging and definition of progression of injury.

Prognostic Factors Assessed in Primary Studies

Twenty-one studies presented within study estimates of effect of individual risk factors on the outcomes of interest (supplementary material 4) and the factors assessed are presented in supplementary material 5. The most influential factors were: age; initial GCS; severity of CT finding; type of injury; anti-coagulation; and anti-platelet medication (Table 2). Individual forest plots are presented in supplementary material 6.

Age

Age was evaluated as a factor in prognostic modelling in 18 primary studies. Ten studies assessed age using 4 different dichotomous cut offs and 11 studies measured age as a continuous factor. Multivariable models included: logistic regression with age either a dichotomised or continuous variable, or decision tree analysis.
Of these 18 studies: six assessed the outcome of clinical deterioration; 8 assessed the outcome of neurosurgery/neurosurgical intervention; 1 measured death as an outcome; and 8 studies evaluated progression of injury on repeat CT imaging. Despite being the most commonly assessed prognostic factor, due to the variation in measurement and the outcomes assessed, it was not possible to undertake a pooled analysis.

Increased age was associated with an adverse outcome in 9 of the 19 univariable models presented. Age was a significant predictor of an adverse outcome in 2 of 5 multivariable models where it was treated as a continuous variable. However, in 4 of 6 multivariable models where it was dichotomised, older age predicted the outcomes of interest. This may indicate a non-linear relationship with older age groups having a disproportionately higher associated risk of adverse outcomes.

Initial GCS

Twelve primary studies presented within study estimates of the effect of initial GCS on the risk of the outcomes of interest. Univariable effect estimates of initial GCS 15 were pooled for studies assessing clinical deterioration and neurosurgery/neurosurgical intervention as an outcome with individual patient data provided by Fabbri et al and an initial GCS=15 was protective against clinical deterioration or neurosurgery/neurosurgical intervention (pooled OR 0.35 95% CI: 0.23 to 0.53) (Table 2). Two papers assessed progression of injury on repeat CT imaging and both found initial GCS 15 to be associated with reduced risk of progression. Four studies estimated the effect of an initial GCS of 15 in multivariable models. All 4 multivariable models found initial GCS15 to be associated with a reduced risk of adverse outcomes.

Severity of Injury as assessed by CT findings

Nine studies estimated whether the severity of injury identified by initial CT scan predicted adverse outcomes. This was assessed by: the presence of midline shift or mass effect in 5
studies, 6, 55, 66, 76, 100 the Marshall classification in 2 studies, 41, 73 and measures of haemorrhage thickness or volume in 4 studies, 54, 55, 78, 100 The variability in the measures of injury severity and differences in the outcomes assessed prevented pooling. All studies that assessed presence of midline shift/mass effect found it to be statistically predictive of adverse outcomes. This association remained in the 2 studies that presented multivariable analysis. 6 The Marshall classification was assessed as a continuous and dichotomised variable 41 and neither study found a statistically significant association with adverse outcomes. The 2 studies which assessed the effect of bleed thickness>10mm found this to be statistically predictive of either progression of injury on repeat CT imaging or neurosurgical intervention in both uni and multivariable analysis. 54, 78

Isolated subarachnoid haemorrhage

Twelve studies presented outcomes for populations with isolated injuries and patients with isolated subarachnoid haemorrhages (iSAH) were the lowest risk for adverse outcomes:

neurosurgical intervention pooled risk 0.01% (95% CI: 0 to 0.7%) (Fig. 11), and 1.1% (95% CI: 0 to 5.5%) pooled prevalence of clinical deterioration (supplementary material 7). 32, 37, 55, 59, 71, 74, 77, 98, 99, 103, 107, 108

Univariable effect estimates presented in the 2 studies that assessed the effect of the presence of iSAH were pooled with data extracted from 3 additional studies. 37, 73, 77, 98, 108 The pooled estimate indicated iSAH reduced the risk of neurosurgical intervention/clinical deterioration (Table 2).

Two multivariable models included iSAH as a prognostic factor. One found iSAH to be associated with a lower risk of clinical deterioration. 37 The other found iSAH to have no effect on risk. 98

Isolated extradural haemorrhage
Patients with isolated extradural haemorrhage had the highest risk of neurosurgery/neurosurgical intervention: 13.7% (95% CI: 9.3% to 18.5%) (Fig. 11). 18.5% is estimated from a population of all initial GCS14-15 patients with extradural haemorrhage, whilst the estimates in the other studies are from populations that have been selected for more conservative management. 77, 98, 107, 108

Three studies assessed isolated extradural haemorrhage as a prognostic factor. 37, 73, 98 A pooled risk estimate for clinical deterioration or neurosurgery/neurosurgical intervention using these 3 studies and outcome data extracted from a further 2 studies, 77, 108 found isolated extradural haemorrhage to be associated with these outcomes (OR 2.26 95% CI: 1.9 to 2.68) (Table 2). Isolated extradural haemorrhage remained statistically associated with neurosurgical outcomes in the only multivariable model that included this factor. 98

Anti-coagulation

Twelve studies estimated the prognostic effect of anti-coagulation. 6, 37, 41, 55, 74-76, 78, 98, 100, 101, 139 Measures of anti-coagulation included: any documented coagulopathy, 6, 41, 55, 77, 98, 100 pre-injury warfarin use, 37, 76, 101 warfarin or antiplatelet therapy as a combined risk factor, 78, 100 and continuous laboratory measures of anti-coagulation. 6, 74, 101

Univariable effect estimates of dichotomous measures of anti-coagulation were pooled with individual patient data from Fabbri et al for the composite outcome of clinical deterioration or neurosurgery/neurosurgical intervention (Table 2), pooled estimate: OR 1.45 95% CI: 1.28 to 1.64. Two studies presented multivariable models that included anti-coagulation and it was not statistically associated with the outcomes of interest in either model. 78, 98

Anti-platelet medication

The effect of anti-platelet use was evaluated by: aspirin use, 37, 76, 101 clopidogrel use, 37, 76, 101 and a joint measure of antiplatelet use. 55, 66, 87 No multivariable models included antiplatelet use. Pooled univariable risk estimates of pre-injury aspirin and clopidogrel use are presented in Table 2. Meta-
analysis indicated a statistical association between clopidogrel with clinical deterioration or neurosurgical intervention but no association between aspirin use and this outcome.

Discussion:

Summary

We have completed a thorough systematic review and meta-analysis to identify risk factors for adverse outcomes in this TBI population. This is the first review to provide pooled estimates of clinically important outcomes in this population and identify which factors affect the risk of these outcomes.

The pooled prevalence of adverse outcomes were: 11.7% (95% CI: 8.21 to 5.8%) clinical deterioration, 3.5% (95% CI: 2.2 to 4.9%) neurosurgical intervention, and 1.4% (95% CI: 0.8% to 2.2%) death. These outcome estimates used a pooled total of 65724 patients and are comparable to the 2.7% craniotomy rate reported for a similar population in a national UK trauma database.141 The variation in individual study outcomes reflects differences in populations studied and outcome definitions. For the outcomes of neurosurgical intervention and death heterogeneity could be explained by the age of study populations and different study population GCS scores.

Risk factors for adverse outcomes were identified using both meta-regression of study characteristics and synthesis of prognostic models presented by primary studies. Age, anti-coagulation and initial GCS were found by both methods to affect risk. An increase in mean study population age by 1 year was associated with increased odds of neurosurgery/neurosurgical intervention of 1.09 in multivariable meta-regression (Table 1) and age was a predictor of an adverse outcome in 6/11 multivariable models presented in primary studies. In univariable meta-regression a unit increase in the percentage of the study population taking anti-coagulants was associated with a 1.1 increase in the odds of neurosurgery/neurosurgical intervention (Table 1). Pooling of univariable
models presented in primary studies found anticoagulated patients to have odds 1.45 time greater than patients not anticoagulated for neurosurgical intervention/clinical deterioration (Table 2). In multivariable meta-regression, a unit increase in mean/median study population GCS was associated with a 0.12 reduction in the odds of neurosurgical intervention (Table 1). Pooling of univariable models indicated that patients with initial GCS < 15 had odds of clinical deterioration/neurosurgical intervention 2.9 times that of less than patients that presented with an initial GCS of 15 lower GCS scores (Table 2). In multivariable meta-regression models including both initial GCS and age, initial GCS had a smaller effect on the risk of either neurosurgical intervention or death than in univariable analysis and this may be due to older patients presenting with higher initial GCS relative to the severity of their injury (Table 1). Patients with extradural haemorrhage had the highest prevalence of adverse outcomes, whilst patients with isolated subarachnoid haemorrhage had the lowest (Fig. 11).

Meta-analysis of multivariable models was not possible due to the small number and variability in how these models were constructed. Therefore, although this review has identified the factors that affect risk, no model that could identify low-risk patients was found or could be reliably constructed.

**Strengths**

A thorough search has been conducted, identifying 50 relevant primary studies. Our review fulfils all the AMSTAR systematic review checklist quality domains apart from items 10 and 11, regarding the assessment of publication bias and conflicts of interest. However, the non-interventional nature of the included studies means these domains are less relevant. This review is low-risk for bias in the 5 domains assessed by the Risk of Bias in Systematic reviews (ROBIS) tool.

**Limitations**

Many studies identified were small and retrospective with limited follow up of patients after discharge. Instead of attempting to identify low-risk patients through prognostic modelling, several
studies selected patients on study specific characteristics for different care pathways. This variation
in study populations contributed to heterogeneity in estimates of outcome prevalence and risk
factor effect. The prognostic models that were identified were often derived in cohorts too small to
construct multivariable models with all relevant factors. The clinically useful outcome in informing
discharge decisions is clinical deterioration, and most prognostic models did not assess this.

Clinical deterioration was defined by 7 different composite outcomes and most commonly by
neurological deterioration. This lack of consistency in definition contributed to the heterogeneity in
outcome estimates. Neurological deterioration was variably defined and a clinically relevant and
consistently used definition or deterioration is required.

No included studies assessed pupillary response and duration of loss of consciousness/amnesia.
These factors are predictive of adverse outcomes in other TBI populations and future research
should assess these factors in this population.\textsuperscript{13, 143}

\textit{Context}

When the Canadian CT Head Rule was developed, the authors presented a consensus derived list of
intra-cranial injuries that would never require \textit{neurosurgical intervention}.\textsuperscript{4} The
implication was that patients with such injuries were safe for discharge. This was rejected by the
Society of British Neurological Surgeons.\textsuperscript{1} A US group based in Arizona has produced the BIG
consensus derived statement that identifies a population with low risk clinical characteristics and
intra-cranial injuries similar to those presented by the CCHR authors.\textsuperscript{109} They propose such patients
are safe for discharge after 6 hours of ED observation.\textsuperscript{9, 27, 109}

Kreitzer et al present an alternative policy at a level 1 trauma centre in Cincinnati where the
population of interest remain in the ED for observation and undergo repeat CT imaging
approximately 6 hours following diagnosis.\textsuperscript{86} Neurologically stable patients without progression of
injury are discharged. Pruitt et al present a model of care in a Level 1 trauma centre in Chicago in
which all GCS13-15 patients with intra-cranial injuries receive a neurosurgical consultation. Low
risk patients identified by the neurosurgeon are left under ED care and discharged after a period of
observation. This is similar to the standard of care in the UK NHS.

Others advocate the admission of all GCS13-15 patients, and with brain injuries identified by CT
imaging to higher levels of care and routine re-imaging, citing evidence that deterioration in
neurological examination may not identify progression of injury that warrants clinical intervention.

Multiple reviews have found that this too rare an occurrence to warrant routine re-imaging of all
GCS13-15 patients with TBI identified by CT.

Implications

This review supports the view that there are subsets of GCS13-15 patients with injuries identified by
CT imaging that may possibly be safely routinely discharged from the ED. However, the current
available evidence is insufficient to reliably identify such low-risk patients. The risks of serious
adverse outcomes are sufficiently high that, in the absence of evidence to be able to accurately pin
point low-risk individual patients, admission for observation probably remains clinically indicated.

No validated model predicting a measure of clinical deterioration that could be used to triage
hospital admission was identified. We suggest future research should assess a measure of clinical
deterioration that encompasses: neurosurgery, neurosurgical intervention, death, a fall in GCS by 2 or
more points, seizure activity, intravenous medical intervention or ICU intervention. These would
warrant ongoing inpatient hospital admission.

The BIG criteria, although the best effort at risk stratifying this group in a clinically relevant way,
require validation in larger prospective cohorts in different healthcare contexts before being more
widely adopted. They were derived by consensus, and empirical prognostic modelling could possibly
improve the accuracy of risk stratification.
Decision rules have been employed successfully in the ED to risk stratify patients in a range of conditions, including ankle injuries and suspected pulmonary embolus.\textsuperscript{144, 145} Equivalent models could be used for patients with mTBI to identify low-risk patients. This review has identified the key factors that are likely to inform such risk stratification, but an adequately powered derivation study with a clinically relevant definition of deterioration and adequate follow up is required.

**Conclusion**

Mild TBI patients with injuries identified by CT imaging are a heterogeneous group. Their overall risk of clinical deterioration and more serious adverse outcomes is small, but clinically significant. Current research gives an indication to which factors affect the risk of adverse outcomes but is of too low quality to inform clinical decision making. High quality prognostic modelling is needed to help inform discharge decisions.

**Author Disclosure Statement**

No Competing financial interest exist. Carl Marincowitz is funded by a National Institute for Health Research Doctoral Fellowship. This study presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
References:


scans in patients with intracranial hemorrhage and GCS score of 13 to 15. The Journal of Trauma and Acute Care Surgery 73, 685-688.


Table 1: Meta regression of study factors predictive of death, neurosurgery and clinical deterioration

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<tr>
<th>Factor</th>
<th>Outcome</th>
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<th>Unit Increase Affect Odds Multivariable Model</th>
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<td>Mean Age Study Population</td>
<td>Death</td>
<td>1.05 (95% C.I. 1.0003-1.12) P= 0.049</td>
<td>1.06 (95% C.I. 1.0002-1.12) P= 0.049</td>
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<td>Mean GCS Study Population</td>
<td>Death</td>
<td>0.12 (95% C.I. 0.02-0.86) P=0.04</td>
<td>0.09 (95% C.I. 0.01-0.59) P=0.02</td>
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<td>Lower risk study population versus ICU population</td>
<td>Death</td>
<td>0.27 (95% C.I. 0.08-0.94) P=0.04</td>
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<tr>
<td>Unselected study population versus ICU population</td>
<td>Death</td>
<td>0.81 (95% C.I. 0.22-1.97) P=0.63</td>
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<td>Percentage population Anticoagulated</td>
<td>Death</td>
<td>1.05 (95% C.I. 0.95-1.17) P=0.32</td>
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<td>1.09 (95% C.I. 1.02-1.16) P=0.02</td>
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<td>Mean GCS Study Population</td>
<td>Neurosurgery</td>
<td>0.71 (95% C.I. 0.01-0.56) P=0.01</td>
<td>0.12 (95% C.I. 0.02-0.91) P=0.04</td>
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<td>Lower risk study population versus ICU population</td>
<td>Neurosurgery</td>
<td>0.13 (95% C.I. 0.04-0.41) P&lt;0.01</td>
<td>0.67 (95% C.I. 0.10-4.37) P=0.66</td>
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<td>0.95 (95% C.I. 0.43-2.12) P=0.90</td>
<td>1.34 (95% C.I. 0.45-4.02) P=0.58</td>
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<td>Percentage population</td>
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<td>0.63 (95% C.I. 0.27-1.43) P=0.26</td>
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Table 2: Summary of effect estimates of risk factors assessed within studies

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<td>Initial GCS 15</td>
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<td>Severity CT brain</td>
<td>9, 81, 54, 56, 73, 76, 78, 100</td>
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<td>Isolated SAH</td>
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<td>Isolated EDH</td>
<td>5, 73, 77, 98, 108</td>
<td>OR 2.26 95% CI: 1.9 to 2.68</td>
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<td>Isolated SDH</td>
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<td>Isolated Contusion</td>
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<td>Anti-coagulation</td>
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<td>Aspirin</td>
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*Pooled estimate of effect on risk of neurosurgery or clinical deterioration

**Indicates number of multivariable models where factor was found to be a significant predictor and direction of effect on risk
PRISMA Flow Diagram

Records identified through database searching (n = 4665)  Additional records identified through other sources (n = 178)

Records after duplicates removed (n = 4431)

Records screened (n = 4431)  Records excluded (n = 4308)

Full-text articles assessed for eligibility (n = 123)  Full-text articles excluded, with reasons (n = 69)

Studies included in qualitative synthesis (n = 49) + 5 Reviews

Studies included in quantitative synthesis (meta-analysis) (n = 45) + 1 review

Figure 1

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Figure 2

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Figure 3

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Figure 4

120×95mm (300 x 300 DPI)
Figure 6

128x98mm (300 x 300 DPI)
Figure 7

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Figure 8

101x68mm (300 x 300 DPI)
Figure 9

166x192mm (300 x 300 DPI)
Figure 10

181x213mm (300 x 300 DPI)
Figure 11

194x237mm (300 x 300 DPI)
Figure 1: PRISMA flow-diagram showing selection of studies for inclusion in the systematic review

Figure 2: Risk of Death stratified by initial GCS

Figure 3: Meta-regression risk of death by mean age study population (Coefficient odds 1.05 (95% CI: 1.00 to 1.12) P=0.049)

Figure 4: Meta-regression risk of death by mean GCS study population (Coefficient odds 0.12 (95% CI: 0.02 to 0.86) P=0.04)

Figure 5: Risk of neurosurgery stratified by the initial GCS of the study population

Figure 6: Meta-regression of risk of neurosurgery by mean GCS study population (Coefficient odds 0.71 (95% C.I. 0.01- 0.56) P=0.01)

Figure 7: Meta-regression of risk of neurosurgery by mean age study population (Coefficient odds 1.01 (95% C.I. 1.02- 1.11) p=0.01)

Figure 8: Meta-regression of risk of neurosurgery by percentage of study population taking anti-coagulants (Coefficient odds 1.1 (95% C.I. 1.01-1.19) p=0.04)

Figure 9: Estimates of clinical deterioration stratified by the outcome measure

Figure 10 Risk on repeat CT imaging of progression of injury stratified by whether entire population selected for repeat imaging

Figure 11: Pooled risk of neurosurgery stratified by isolated injury type identified by initial CT imaging
Supplementary material 1: Full Search Strategy

Embase search 24/11/2016 1996 to 2016 Week 47:

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<td>S1    head injury</td>
<td>View Results (7,746)</td>
</tr>
</tbody>
</table>
Cochrane CENTRAL:

Search Name: Prognostic systematic Review
Date Run: 24/11/16 11:33:55.251

<table>
<thead>
<tr>
<th>ID</th>
<th>Search</th>
<th>Hits</th>
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<tbody>
<tr>
<td>#1</td>
<td>Craniocerebral Trauma</td>
<td>417</td>
</tr>
<tr>
<td>#2</td>
<td>head injury</td>
<td>2563</td>
</tr>
<tr>
<td>#3</td>
<td>#1 or #2</td>
<td>2704</td>
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<tr>
<td>#4</td>
<td>Hematoma, Subdural</td>
<td>228</td>
</tr>
<tr>
<td>#5</td>
<td>Hematoma, Epidural, Cranial</td>
<td>20</td>
</tr>
<tr>
<td>#6</td>
<td>Cerebral Hemorrhage</td>
<td>2609</td>
</tr>
<tr>
<td>#7</td>
<td>Skull Fracture</td>
<td>130</td>
</tr>
<tr>
<td>#8</td>
<td>Skull Fracture, Basilar</td>
<td>6</td>
</tr>
<tr>
<td>#9</td>
<td>Skull Fracture, Depressed</td>
<td>13</td>
</tr>
<tr>
<td>#10</td>
<td>brain contusion</td>
<td>131</td>
</tr>
<tr>
<td>#11</td>
<td>#4 or #5 or #6 or #7 or #8 or #9 or #10</td>
<td>2969</td>
</tr>
<tr>
<td>#12</td>
<td>#3 and #11</td>
<td>211</td>
</tr>
</tbody>
</table>

All Results (211)

- [ ] Cochrane Reviews (138)
- [ ] All Review Protocol
- [ ] Other Reviews (4)
- [ ] Trials (63)
- [ ] Methods Studies (0)
- [ ] Technology Assessments (0)
- [ ] Economic Evaluations (1)
- [ ] Cochrane Groups (5)

Only trials retrieved.
### Supplementary Material 2: Data Extracted from Included Studies

#### Studies Only Included in Meta-Analysis of Prevalence of Outcomes N=26

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Study Design</th>
<th>Outcome Measures</th>
<th>Prognostic factors assessed</th>
<th>Results</th>
<th>Quality Appraisal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nishijima et al 2013 Sacramento USA</td>
<td>Multicenter-8 sites Western USA. All Level I Trauma registries searched for ICD-9 codes intra-cranial haemorrhage 2005-2010</td>
<td>Retrospective Cohort Study</td>
<td>Initial ICU admission from ED</td>
<td>Age</td>
<td>11240 patients coded as bleeds</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Proportion of patients receiving crit care intervention defined as:</td>
<td>Initial GCS</td>
<td>771 excluded due to missing data</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neurosurgical intervention</td>
<td>Initial BP</td>
<td>1412 remaining met inclusion criteria.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mechanical ventilation</td>
<td>LOS hosp</td>
<td>888/1412 admitted ICU, significant variation between sites</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vasopressor/ionotropic use</td>
<td>ICU stay</td>
<td>44/1412 (3.1%) had critical care intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Transfusion blood product</td>
<td>Procedures as coded in trauma registry</td>
<td>6/1412 neurosurgical intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Invasive monitoring</td>
<td>AIS</td>
<td>847/888 patients admitted ICU no crit care intervention</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Mean/median GCS=15</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Mean/median age= 48</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Study Recruitment: Mod risk bias</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Dependent on accuracy on recording on trauma registry. Does have some quality assessment of data imputation</td>
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<tr>
<td></td>
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<td>Note initial GCS 15- lower risk group</td>
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<td></td>
<td></td>
<td>Attrition: Low risk</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Follow up only during hospital admission</td>
<td></td>
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<td></td>
<td>Prognostic factor measurement: Low risk</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Doesn’t really apply as testing disposition not outcomes</td>
<td></td>
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<td></td>
<td>Outcome measures: Low risk</td>
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<tr>
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<td></td>
<td>No measure of outcomes after discharge, but study primarily about disposition. Does not report deaths.</td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td>Confounding Factors:</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>States IIS increases ICU admission= will be related to other injuries</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Statistical techniques: low risk N/A</td>
<td></td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>Overall</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Only GCS15 patients with low ISS.</td>
<td></td>
</tr>
<tr>
<td>Nishijima et al 2015 Sacramento USA</td>
<td>Level1 trauma centre 2008-2013</td>
<td>Retrospective Cohort Study</td>
<td>Prospective long term outcome measure at 6 months</td>
<td>age sex, mechanism of injury initial ED GCS score, initial (SBP) heart rate, respiratory rate, blood alcohol level, AIS score ISS score INR</td>
<td>188 met inclusion criteria</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Long-term Neurological Outcomes in Adults with</td>
<td></td>
<td></td>
<td></td>
<td>151/188 complete data= cohort</td>
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</tr>
<tr>
<td></td>
<td>Isolated Head Injury based on AIS score</td>
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<td>106 admitted ICU (70%)</td>
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<td>45 admitted ED (30%)</td>
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<td></td>
<td>1/151 patients neurological intervention as inpatient</td>
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<td>1/151 patient died as inpatient</td>
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<td>78 (52%) GOS-E 8 at 6 months</td>
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<td>Does present analysis for outcome at 6 months GOSE but no inpatient measures of deterioration.</td>
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<td>Study Recruitment: Mod risk bias</td>
<td></td>
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<td></td>
<td>Dependent on accuracy on recording on trauma registry and accuracy of case notes.</td>
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<td></td>
<td>Low risk group- GCS 15 and benign CT</td>
<td></td>
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<td></td>
<td>Attrition: Low risk</td>
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<td></td>
<td></td>
<td>Loss of 37 patients to follow up</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Prognostic factor measurement: Low risk</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>As recorded in case notes so dependent on accuracy</td>
<td></td>
</tr>
</tbody>
</table>
## Traumatic Intracranial Hemorrhage Admitted to ICU versus Floor

### Table:Outcome measures: Low risk
- Prospective follow up by trained staff using validated tool. Not clear what would happen to patients who died or deteriorated and attended a different hospital.

### Table: Confounding Factors:
- Patients which are perceived as higher risk will be put on ICU, likely to be differences in comorbidities

### Table: Statistical techniques: low risk
- Well presented- not really relevant to meta-analysis

### Table: Only GCS15 patients with benign looking CT scans

### Table: Schaller et al 2015

<table>
<thead>
<tr>
<th>Center</th>
<th>Level 1 Trauma centre</th>
<th>Bern Switzerland</th>
<th>Jan 2006-Dec 2007</th>
</tr>
</thead>
</table>

#### Inclusion criteria:
- Admission GCS 13-15
- Observed for 24H
- Localised intracranial bleeds up to 5mm: this is from the CCHR paper

#### Exclusion Criteria:
- Bleeds > 5mm maximum diameter
- Multiple bleeds
- History of bleeding tendency
- Anti-coagulant or anti-platelet medication
- Intoxication

#### Summary:
- Retrospective cohort study/case series
- Aim to assess if a specific group of patients with small bleeds can be discharged from hospital without 24 hours of observation
- Deterioration in neurological status or need for neurosurgery
- Prognostic factors are the inclusion/exclusion criteria
- No comparison in risk of deterioration in 2 groups
- 110 patients met inclusion and exclusion criteria.

#### Results:
- None deteriorated within the period of hospital observation, required neurosurgery or re-attended.
- Mean/median GCS=14.6
- Mean/median age= 40
- Percent anticoagulated=0

#### Study Recruitment: Low risk bias
- Retrospective cohort review- reliant on accuracy of written notes.

#### Attrition: Mod risk
- Patients may have moved out of catchment area of hospital without the researchers being aware. Loss to F/U if re-presented different hospital.

#### Prognostic factor measurement: Mod risk
- Reliability of case notes- may be incomplete
- Interpretation size of the bleed was taken from written radiology report ?reliability.

#### Outcome measures: Moderate risk
- Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration. Not clear how patients died in the community would have been identified.

#### Confounding Factors: Low risk
- No obvious confounding factors
- Cohort selection criteria including not living
<table>
<thead>
<tr>
<th>Levy et al 2011</th>
<th>Level 1 Trauma centre Denver USA Jan 1998-Dec 2008</th>
</tr>
</thead>
</table>
| Inclusion criteria: | - Admission ED GCS 13-15  
- On trauma registry  
- Blunt head trauma  
- ICD 850-850.99- consistent with concussion (i.e. no detected injury by CT)  
- Admitted to hospital  
- AIS score 2 before 2008 or 1/2 in 2008  
- IC9 code for SAH  
- Exclusion Criteria: | - Patient admitted directly to hospital  
- Multiple injuries AIS score >1 head or other regions  
- Age less than 18  
- Not admitted |
| Retrospective Cohort Study | ED disposition  
- ICU admission  
- Neurosurgery  
- In-hospital mortality  
- Progression of SAH on CT |
| Aim | To assess whether patients admitted with CT –VE mTBI have different outcomes to patients with mTBI and traumatic SAH  
Univariate and multivariate regression used to examine covariates and relationship to outcomes |
| Age (18-39)(40-69)(70+)|  
- Transfer status  
- Cause of injury  
- GCS  
- Blood alcohol level  
- Presence of skull fracture  
- CT report- divided into small/medium/large based on language included in report |
| 1144 patients admitted with mTBI but negative CT scan | 17 with mTBI and traumatic SAH  
1/117- progression on repeat CT scan  
0/117 required neurosurgical intervention  
1/117 died (progression on CT)  
4/1144 died |
| All patients died >70 |
| Logistic regression model tSAH versus concussion |  
- ICU admit adjusted OR 8.87 (5.62-14.02) P<0.0001  
- ICU LOS>1D OR0.29 (0.11-0.74) P=0.01  
- Hosp LOS>1D OR1.07 (0.67-1.69) P=0.79  
- Mortality OR2.46 (0.27-22.17) P=0.42  
- Discharge to rehab  
- Age18-39 OR5.48 (0.25-121.70) P=0.28  
- Age 40-69 7.96 (1.91-33.11) P=0.004  
- Age >70 1.33 (0.50-3.53) P=0.56 |
| Study Recruitment: Low risk bias | Patients recruited from trauma registry depends on how good this is |
| Only admitted patients- higher acuity patients then discharged.  
Likely patients admitted for other reasons if CT negative TBI (although excludes other injuries). |
| Attrition: Low risk | All inpatient outcomes |
| Prognostic factor measurement: Mod risk | CT findings abstracted from CT reports- severity assigned by language- not actually used in regression model |
| Outcome measures: Moderate risk | Only inpatient outcomes- possibility of discharge and deterioration. |
| Confounding Factors: High risk | Patients admitted with CT negative TBI likely to be frail or have other reasons for admission- this will affect outcome measures compared to SAH patients admitted due to +ve CT. |
| Statistical techniques: Low risk | Well presented. |
Levy et al 2014

<table>
<thead>
<tr>
<th>Study</th>
<th>Level III rural non-neurosurgical unit in Rocky mountains April 2007-Dec 2012</th>
<th>Retrospective cohort Study</th>
<th>Length of stay</th>
<th>No comparison to patients that were transferred</th>
<th>76/273 patients not transferred &gt;50% injuries due to skiing/snow boarding 71% patients less then 55</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim</td>
<td>Investigate outcomes after a novel non-transfer policy for mTBI patients with small ICH introduced in a small rural trauma unit without neurosurgical cover</td>
<td>Mortality Neurological deterioration Neurosurgery Re-admission in 90 days of discharge Inter-hospital transfer Need for repeat CT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inclusion criteria:</td>
<td>Admission GCS 13-15 CT positive intracranial injury Not transferred to neurosurg unit in accordance with non-transfer policy. CT findings of small SAH Punctate or minimal contusion Punctuate or minimal intra-</td>
<td></td>
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</tr>
<tr>
<td>Study Recruitment: Low risk bias Retrospective cohort review- reliant on accuracy of written notes. CT inclusion criteria are subject and patients may have been transferred despite meeting non-transfer policy if clinicians were concerned. Attrition: low risk Prognostic factor measurement: Mod risk Reliability of case notes- may be incomplete The definitions of bleed size are subjective. Prognostic Factors N/A</td>
<td></td>
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</tr>
<tr>
<td>Outcome measures: Moderate risk Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration. Confounding Factors: Low risk Age affect outcome and size of bleed Statistical techniques: N/A</td>
<td></td>
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</tr>
</tbody>
</table>

Can use for pooling for outcomes SAH supports low risk sub-population
### General points

- Small numbers.
- No comparator group—need to compare to transferred patients outcomes.
- Patient not generalizable—v. young and atypical mechanism of injury (mostly winter sports related).
- Likely that any patient clinicians felt risky would have been transferred even if did not meet transfer criteria—no way to check this.

## Joseph et al 2013 USA

**The acute care surgery model: Managing traumatic brain injury without an inpatient neurosurgical consultation**

<table>
<thead>
<tr>
<th>Inclusion criteria:</th>
<th>Exclusion Criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS 13-15</td>
<td>Any coagulopathy</td>
</tr>
<tr>
<td>Trauma</td>
<td>Basilar skull fracture or evidence of CSF leak</td>
</tr>
<tr>
<td>Positive findings CT skull fracture and/or ICH</td>
<td>Extra-dural bleed</td>
</tr>
<tr>
<td>Pre-hospital anti-platelets or anti-coagulants</td>
<td>Any significant contusion or SDH/intra-cerebral haemorrhage</td>
</tr>
</tbody>
</table>

**Hypothesis**

Trauma surgeons can manage mTBI patients with CT detected intracranial haemorrhage without neurosurgical consultation.

**Retrospective cohort study—propensity matching 1:2 ratio patients managed solely by trauma surgeons versus patients that had neurosurgical consultation.**

**Hospital admissions**

<table>
<thead>
<tr>
<th>Inpatient ICU admissions</th>
<th>Neurosurgical interventions</th>
<th>ED visits after discharge</th>
<th>Mortality</th>
<th>Progression on CT imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>404-GCS 13-15 patients with CT detected injuries in study period.</td>
<td>270/404 used for this study</td>
<td>90/270—had neurosurgical consultations (NC)</td>
<td>180 no neurosurgical consultation. (no-NC)</td>
<td>0/270 neurosurgical interventions, hospital mortality or readmissions either group.</td>
</tr>
<tr>
<td>78/90 no-NC and 158/180 NC admitted hospital (P=0.8)</td>
<td>18/90 no-NC and 80/180 NC admitted ICU (P=0.001)</td>
<td>Routine repeat CT 18/90 no-NC 155/180 NC (P&lt;0.001)</td>
<td>No progression on any repeat CT</td>
<td>8% no-NC and 4% NC group re-attended ED. No readmissions.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Initial GCS</th>
<th>ISS</th>
<th>Head-abbreviated injury score</th>
<th>Neurological examination CT scan findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>404-GCS 13-15 patients with CT detected injuries in study period.</td>
<td>270/404 used for this study</td>
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<td>8% no-NC and 4% NC group re-attended ED. No readmissions.</td>
<td></td>
</tr>
</tbody>
</table>

**Prognostic factor measurement: Low risk**

All routinely collected clinical data apart from CT imaging which re-reviewed.

**Outcome measures: Mod risk**

Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration.

**Confounding Factors: Mod risk**

Does not exclude patients with additional injuries.
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Setting</th>
<th>Year</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Hypothesis</th>
<th>Outcome measures during hospital admission</th>
<th>Comparison between groups</th>
<th>Outcome</th>
<th>Statistical techniques</th>
<th>Attrition</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbdelFattah et al. 2012</td>
<td>USA</td>
<td>Level 1 trauma center Dallas Texas</td>
<td>2010-2011</td>
<td>Adult with ICH (note doesn’t explicitly state 2ndary to trauma- but implied)</td>
<td>Age&lt;16, GCS&lt;13, Undergone planned or immediate neurosurgery, Transferred patients</td>
<td>Repeat CT imaging in GCS13-15 with ICH, without neurological progression, does not impact the need for neurosurgical intervention. Patients divided into those 2 groups. Patients with planned repeat CT imaging and those with CT imaging if deteriorated. Allocation by neurosurgeon-no deviation from normal practice.</td>
<td>Neurologic progression, Medical intervention, Neurosurgical intervention, Repeat CT imaging- worse CT defined as worse by a blinded radiologist/neurosurgeon giving qualitative measure of bleed.</td>
<td>Age, Sex, Coagulation status, Anti-platelets, ISS, GCS</td>
<td>Mean/median GCS=14.5, Mean/median age=41, Percent anticoagulated=6</td>
<td>High risk</td>
<td>Small numbers. Likely reporting data reported elsewhere.</td>
<td></td>
</tr>
<tr>
<td>Nayak et al. 2013</td>
<td>USA</td>
<td>University Hospital Newark New Jersey Level 1 trauma centre 2003-2008</td>
<td></td>
<td></td>
<td></td>
<td>Neurosurgical intervention after 24 hours- craniotomy, ventriculostomy, ICP bolt/measurement, Death in hospital</td>
<td>Age, Sex, Mechanism of Injury, GCS on admission ISS, HAIS</td>
<td>321/864 patients GCS13-15 with ICH met inclusion criteria, 20% excluded because incomplete medical notes/transfers</td>
<td>Low risk</td>
<td>Small study with confounders regarding outcomes.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Statistical techniques:**
- High risk: Does not outline how matched groups using propensity scoring.
- Low risk: None

**Attrition:**
- Low risk: Follow up only for period in hospital.
- Mod risk: No F/U following discharge- missed delayed outcomes, could have looked for re-attendance.

**Confounding Factors:**
- High risk: Not isolated head injury- other injuries have clearly affected outcome measures.
- Low risk: None

**Prognostic factor measurement:**
- Low risk: Blinded appraisal of CT scans by researcher.

**Outcome measures:**
- Mod risk: Neurologic outcomes of MHI patients with an intra-cranial bleed
- Low risk: No F/U following discharge- missed delayed outcomes.
### Study by Anandalwar et al. 2016

**University Hospital Newark New Jersey USA**

**Inclusion criteria:**
- Aged 18 and over
- Blunt trauma
- Intra-cranial bleed
- Admitted to hospital
- GCS 13-15 on arrival to ED
- GCS 15 24 hours after attendance to ED

**Excluded:**
- History brain disease, e.g. dementia
- Previous brain injury e.g. CVA
- Liver cirrhosis, renal disease, coronary artery disease, bleeding or clotting disorder
- Unable to assess GCS due to drugs e.g. sedation/intubation
- Neurological deterioration leading to repeat CT
- Aged less than 15
- Incomplete notes

### Study Recruitment: High risk

Patients at GCS 15 at 24 hours- low risk group selected out- difficult to extrapolated to all GCS 13-15 patients.

### Attrition: Low Risk

- No compare outcomes in patient that adhered to and violated non-routine repeat CT head imaging. Potentially clinicians ordered routine repeat CT imaging on riskier patients.

### Prognostic factor measurement: Mow risk

Neuroradiology reports taken at face value-no verification

### Outcome measures: mod risk

- No uniform follow up of patients post discharge. Some patients had F/U clinic others didn’t. Patients may presented after discharge to other sites.

### Confounding Factors: low risk

- None obvious

### Statistical techniques: Low risk

- None completed

The inclusion/exclusion criteria have selected out all patients that are not GCS 15 at 24 hours. Different population than all GCS 13-15 patients with TBI on CT- probably unable to pool this data.

Does show patients that are GCS 15 at 24 hours low risk.

### Aim

Assess the outcomes following the implementation of a policy of observation only (no repeat CT imaging) for GCS 15 patients.

### Retrospective cohort study

**Repeat CT after 24 hours of admission due to clinical concern or deterioration.**

**Progression on any repeat CT completed.**

**Neurosurgical interventions.**

**Intubation, ICU admissions, administration of mannitol.**

### Age

- 533 patients TBI and ICH
- 142 met the inclusion/exclusion criteria
- 47 underwent a routine repeat CT within 24 hours (violation of policy): 0/47 neurosurgical, 1/47 had incidental finding on CT
- 95 no repeat routine CT within 24 hours
- 8/95 (non-violation group) had repeat CT >24 hours after admission- due to concern.
- 3/8 progression on CT

### Study Recruitment: High risk

**Repeat CT after 24 hours of admission due to clinical concern or deterioration.**

**Progression on any repeat CT completed.**

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- 8/95 (non-violation group) had repeat CT >24 hours after admission- due to concern.
- 3/8 progression on CT
<table>
<thead>
<tr>
<th>Hospital</th>
<th>ED revisits within 1 year for TBI related symptoms.</th>
<th>1 neurosurgical intervention</th>
<th>Potential for patients to have re-attended at other EDs and be missed</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>2/8 admitted to ICU due to deterioration- 1 intubated</td>
<td>Mean/median GCS=14.8</td>
<td>Prognostic factor measurement: Low risk</td>
</tr>
<tr>
<td>of</td>
<td>3/95 patients returned with 1 year to the ED due to TBI</td>
<td>Mean/median age= 38</td>
<td>No risk model developed</td>
</tr>
<tr>
<td>neurological disorder</td>
<td>symptoms- all underwent repeat CT. No admissions.</td>
<td>Percent anticoagulated=0</td>
<td>Factors abstracted from case notes</td>
</tr>
<tr>
<td>Immediate</td>
<td></td>
<td></td>
<td>Outcome measures: low risk</td>
</tr>
<tr>
<td>neurosurgery</td>
<td></td>
<td></td>
<td>Re-attendance at other EDs makes re-attendance a potentially biased outcome measure</td>
</tr>
<tr>
<td>Previous TBI or neurosurgery</td>
<td></td>
<td></td>
<td>Confounding Factors: Mod risk</td>
</tr>
<tr>
<td>Spinal injury</td>
<td></td>
<td></td>
<td>Statistical techniques: Low risk</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td></td>
<td></td>
<td>None presented</td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td>Is a lower risk population due to selection for repeat CT imaging and return to GCS15 at 24 hours- possibly unable to include in any meta-analysis.</td>
</tr>
<tr>
<td>Transfers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete notes</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients that did undergo a repeat CT scan despite meeting the rest of inclusion/exclusion criteria formed a comparison group.

<table>
<thead>
<tr>
<th>Study</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
<th>Retrospective Cohort Study</th>
<th>Neurological decline- altered mental state or focal neurological deficit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aim</td>
<td>Assess the clinical implications of SAH or intraparenchymal haemorrhage in mTBI</td>
<td>Neurological decline- altered mental state or focal neurological deficit.</td>
<td></td>
</tr>
<tr>
<td>Inpatient seizure</td>
<td>Delayed neurosurgical evacuation as inpatient.</td>
<td>Neurological decline- altered mental state or focal neurological deficit.</td>
<td></td>
</tr>
<tr>
<td>Inpatient mortality</td>
<td></td>
<td>Neurological decline- altered mental state or focal neurological deficit.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Admission GCS</th>
<th>Anti-coagulation</th>
<th>Anti-platelets</th>
<th>Transfer Distances</th>
<th>Sex</th>
<th>Age</th>
<th>Haemorrhage type</th>
</tr>
</thead>
<tbody>
<tr>
<td>411/500 isolated SAH</td>
<td>63/500 isolated ICH</td>
<td>26/500 both</td>
<td>463 GCS15</td>
<td>30 GCS14</td>
<td>8 GCS13</td>
<td></td>
</tr>
<tr>
<td>469/500 patients pre-hospital medication available</td>
<td>71/469 taking either anti-coagulants or anti-platelets</td>
<td></td>
<td>156/500 transfers</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ditty et al</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria:</td>
<td>500 consecutive patients present on trauma registry</td>
<td>500 consecutive patients present on trauma registry</td>
<td>500 consecutive patients present on trauma registry</td>
<td>500 consecutive patients present on trauma registry</td>
</tr>
<tr>
<td></td>
<td>ICD9 diagnosis SAH and/or intraparenchymal contusion-</td>
<td>ICD9 diagnosis SAH and/or intraparenchymal contusion-</td>
<td>ICD9 diagnosis SAH and/or intraparenchymal contusion-</td>
<td>ICD9 diagnosis SAH and/or intraparenchymal contusion-</td>
</tr>
<tr>
<td></td>
<td>411/500 isolated SAH</td>
<td>63/500 isolated ICH</td>
<td>26/500 both</td>
<td>463 GCS15</td>
</tr>
<tr>
<td></td>
<td>469/500 patients pre-hospital medication available</td>
<td>71/469 taking either anti-coagulants or anti-platelets</td>
<td>156/500 transfers</td>
<td>500 patients met inclusion criteria</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Recruitment: Mod risk</th>
<th>Study Recruitment: Mod risk</th>
<th>Study Recruitment: Mod risk</th>
<th>Study Recruitment: Mod risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>High proportion of transferred patients may represent higher or lower acuity patients than general population.</td>
<td>Higher as being transferred to specialist centre, lower as survived /fit to transfer.</td>
<td>Only inpatient measures</td>
<td>Only inpatient measures</td>
</tr>
<tr>
<td>No details about inclusion or completeness of trauma registry.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Attrition: Low Risk</th>
<th>Attrition: Low Risk</th>
<th>Attrition: Low Risk</th>
<th>Attrition: Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only inpatient measures</td>
<td>Only inpatient measures</td>
<td>Only inpatient measures</td>
<td>Only inpatient measures</td>
</tr>
</tbody>
</table>
confirmed with radiology report and neurosurgical consult note-if disagreement scan re-reviewed if not clear patient excluded
Excluded:
- Diagnosis extra or subdural hematoma
- Penetrating injuries
- Fatal extra-cranial injuries
- CSF leak
- Aneurysmal SAH
- Delayed presentation

No patients had seizures.
No patients had neurological decline.
No patients underwent delayed neurosurgical intervention.
No inpatient mortality

Prognostic factor measurement: Mod risk
Incomplete information regarding medications.
May be other inaccurate recording of factors.
Outcome measures: Mod risk
Only inpatient related outcome measures.
Patients may have been discharged and deteriorated and presented to other hospitals.

Confounding Factors: Mod risk
Cohort includes patients with multiple injuries- only excluded if died from other injuries.

Statistical techniques: N/A
None presented

Narrative synthesis- further evidence SAH low risk.
Deepika et al 2013
Bangalore India

Patients admitted tertiary neurosurgical centre 3 months Jan-March 2010.

Patients identified on a TBI registry
Inclusion criteria:
- GCS 13-15 head injury
- Underwent CT scan
- Either negative CT or isolated traumatic subarachnoid
- Matched comparison between patients -ve CT and SAH

Excluded:
- Does not state

Retrospective cohort study

Aim
To assess whether GCS13-15 patients with traumatic subarachnoid haemorrhage have the same outcomes as mTBI patients with -VE CT scans

Prospective 1 year telephone assessment of:
- GOSE
- Rivermead post concussion questionnaire
- Rivermead head injury follow up questionnaire

Age
Sex
Mechanism of injury
RTC
Fall
LOC
Seizure
Location of SAH
Whether multiple bleeds
Thickness greater or less than 5mm

34/1628 mTBI patients isolated traumatic subarachnoid haemorrhage
18/34 patients available for follow up at 1 year
Good GOSE
Rivermead scores comparable to 16 normal CT controls

Study Recruitment: Low risk
Cohort identified in TBI registry which is part of normal practice.
Is retrospective so limited by accuracy of medical notes.

Attrition: High Risk
Small sample- with large proportion lost to followup.

Prognostic factor measurement: Medium risk
Dependent on CT scan reports and written documentation

Outcome measures: High risk
1 year too long

Confounding Factors: Medium risk
No control for other injuries or comorbidities

Confounding Factors: Low risk
Included patients with polytrauma and significant comorbidities

Statistical techniques: High Risk
None presented but data presented in table and text do not match up

Paper shows patients admitted to hospital by neurosurgeons have worse outcomes/more likely to require neurosurgery.

Does show that in America some of this patient population discharged directly from ED. Consistent with the model used locally in Hull.
<table>
<thead>
<tr>
<th>Kreitzer et al.</th>
<th>Level trauma center</th>
<th>Cincinnati USA</th>
<th>Study Recruitment: Mod risk</th>
<th>Prognostic factor measurement: Medium risk</th>
<th>Attrition: Low Risk</th>
<th>Outcome measures: low risk</th>
<th>Confounding Factors: Low risk</th>
<th>Statistical techniques: N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>2001-2010</td>
<td>Identified from cohort of patients undergone 2 CT within the ED within 24 hours</td>
<td>Identified through repeat CT imaging in ED relies on all of cohort having repeat scans and patients deteriorate and not undergoing second scan being missed</td>
<td>States that some CT are reported by radiology trainees overnight and then corrected by attending radiologists the next day; unable to quantify how much inaccuracy there is. Does state 32% of repeat scan normal</td>
<td>Followed up through social security system for deaths and the rest are inpatient outcome. Possibility of patients re-attending at other ED</td>
<td>Reasonable outcome measures</td>
<td>Controls for comorbidities and other injuries</td>
<td>Too poor quality to include</td>
</tr>
<tr>
<td></td>
<td>Inclusion criteria:</td>
<td>Death within 30 days Neurosurgical intervention within 2 weeks Return to the Ed within 7 days of discharge</td>
<td>After second CT 92/323 admitted 25/323 observed in ED and subsequently discharged 206/323 discharged</td>
<td>States death in discharged patient unlikely to be related to head injury had further fall. Also 1 other patient dies of septic shock.</td>
<td>4 patients died (3 admitted 1 discharged) States death in discharged patient unlikely to be related to head injury had further fall. Also 1 other patient dies of septic shock.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>GCS 14-15 and blunt head injury</td>
<td>CT head findings Age Race Sex Medical background</td>
<td>323/1011 patients that under-went 2 CT head within 24 hours in ED met the inclusion criteria</td>
<td>After second CT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presented within 24 hours injury Intra-cranial bleed first CT defined extradural, subdural, SAH, intra-cerebral and cerebral contusion 2nd CT within 24 hours</td>
<td>Death within 30 days Neurosurgical intervention within 2 weeks Return to the Ed within 7 days of discharge</td>
<td>Underwent 2 CT head within 24 hours in ED met the inclusion criteria</td>
<td>After second CT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excluded: Incomplete notes Pregnant Intubated prior to ED evaluation Abnormal observations Penetrating injury CT scans interpreted at different hospital Coagulopathy either inherited or acquired INR&gt;1.4 (even if taking warfarin) Platelets less than 50 Any non-head injury mandating admission</td>
<td>Statistical techniques: N/A</td>
<td>Study Recruitment: Mod risk</td>
<td>Prognostic factor measurement: Medium risk</td>
<td>Attrition: Low Risk</td>
<td>Outcome measures: low risk</td>
<td>Confounding Factors: Low risk</td>
<td>Statistical techniques: N/A</td>
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<tr>
<td></td>
<td>Retrospective cohort study</td>
<td></td>
<td>Too poor quality to include</td>
<td>Followed up through social security system for deaths and the rest are inpatient outcome. Possibility of patients re-attending at other ED</td>
<td>States that some CT are reported by radiology trainees overnight and then corrected by attending radiologists the next day; unable to quantify how much inaccuracy there is. Does state 32% of repeat scan normal</td>
<td>Reasonable outcome measures</td>
<td>Controls for comorbidities and other injuries</td>
<td>Too poor quality to include</td>
</tr>
<tr>
<td></td>
<td>Standard practice repeat CT at least 6 hours after 1st CT if mTBI with ICH, if CT and patient stable discharge from ED.</td>
<td>28/206 discharged patients returned to ED within 1 week. None re-admitted and some planned removal of sutures.</td>
<td>States death in discharged patient unlikely to be related to head injury had further fall. Also 1 other patient dies of septic shock.</td>
<td>States death in discharged patient unlikely to be related to head injury had further fall. Also 1 other patient dies of septic shock.</td>
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<td>States death in discharged patient unlikely to be related to head injury had further fall. Also 1 other patient dies of septic shock.</td>
</tr>
</tbody>
</table>
### Ding et al. 2012

**Neurosurgical Center, China** 2009-2010

**Inclusion criteria:**
- All patients with TBI with evidence of intra-cranial haemorrhage, some data for GCS 13-15

**Excluded:**
- Immediate neurosurgery
- Died within 3 days
- Severe multiple injuries
- Failed to undergo a repeat CT head

**Study Recruitment:** High risk

**Attrition:** Low Risk

**Prognostic factor measurement:** Medium risk

**Outcomes measures:** Medium risk

**Confounding Factors:** Low risk

**Statistical techniques:** N/A

**Study Design:** Randomized controlled trial

**Aim:** To assess whether neurosurgical review is necessary for patients with traumatic intracranial haemorrhage assigned either to a routine repeat CT or CT only if deterioration

**Demographics:**
- GCS at discharge
- Surgical and medical interventions secondary to CT
- Initial GCS
- Mechanism of injury
- Coagulation INR and platelets

**Surgical and medical management:**
- 32/89 patients in routine CT group GCS 13-15
- 2/32 worse CT scans
- No patients had neurosurgery or altered medical management

**Results:**
- Mean/median age 48

### Huynh et al. 2006

**Level 1 trauma centre, USA** 2004-2005

**Inclusion criteria:**
- mTBI
- Blunt trauma to head
- GCS 15
- Abnormal CT head

**Excluded:**
- Normal initial CT head
- Length of admission less than 48 hours
- Age less than 18

**Study Recruitment:** Medium risk

**Attrition:** Low Risk

**Prognostic factor measurement:** Medium risk

**Outcomes measures:** Medium risk

**Confounding Factors:** Low risk

**Statistical techniques:** N/A

**Study Design:** Retrospective cohort study

**Aim:** To assess whether neurosurgical review is necessary in GCS 15 patients with intracranial injuries

**Demographics:**
- Changes on follow up CT - all patients had routine repeat CT
- Neurosurgical intervention

**Results:**
- 56 patients met inclusion criteria
- 4/56 patients worse repeat CT
- Of these 4:
  - 2/56 patients had fall in GCS to 14 from 15
  - 1/56 given mannitol due to worse CT
  - 1/56 loaded with phenytoin for seizures
- No consistent measure of deterioration
- 0/56 neurosurgical interventions
- 0/56 deaths

**Results:**
- Mean/median GCS=15
- Mean/median age= 41
<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Location</th>
<th>Year</th>
<th>Study Design</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Intervention</th>
<th>Demographics</th>
<th>Statistical techniques: N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almenawer et al 2013</td>
<td>Neurosurgical centre, Ontario, Canada</td>
<td>2006-2011</td>
<td>Retrospective cohort study + meta-analysis to assess whether repeat CT imaging necessary in mTBI with intra-cranial haemorrhage</td>
<td>GCS 13-15 Blunt traumatic head injury Age &gt; 17 Intra-cranial injury CT head Repeat CT scan</td>
<td>No repeat CT scan Previous caniotomy Cranial pathology Coagulopathy Immediate Neurosurgery</td>
<td>Intervention including: Mannitol or hypertonic saline Surgical intervention including ICP bolt or craniotomy</td>
<td>Neurological changes: decrease GCS, cranial nerve change, vomiting and headache</td>
<td>1121 patients with mTBI and ICH 445 met inclusion criteria 91/445 worse CT 21/445 patients neurological outcomes (all preceded by clinical deterioration prior to repeat CT) 4/445 patients medical intervention 2/4 medical outcomes treated with mannitol due solely worse CT other 2 treated due to clinical deterioration. Mean/median GCS = 14.5 Mean/median age = 45 Percent anticoagulated = 0</td>
</tr>
<tr>
<td>Sifri et al 2004</td>
<td>Level Trauma Centre, New Jersey</td>
<td>1999-2001</td>
<td>Retrospective Cohort Study: To assess the value of routine repeat CT imaging in mTBI patients with intra-cranial haemorrhage</td>
<td>GCS 14-15 Blunt traumatic head injury Age &gt; 15 Intra-cranial injury CT head Repeat CT</td>
<td>Excluded:</td>
<td>Worse CT Inpatient neurological deterioration- abnormal neurology- confusion, disorientation or drowsiness Inpatient neurosurgical interventions</td>
<td>CT results as abstracted from radiologist and neurosurgeons reports. Best ED GCS Demographics</td>
<td>243 patients with mTBI and ICH 18/243 excluded as no repeat CT- neurosurgeon ruled insignificant lesion 202/243 included as met the rest of inclusion criteria At 24 hours: 151/202 persistently normal or improving neurology 51/202 persistently abnormal or worsening neurological examination</td>
</tr>
<tr>
<td>Study</td>
<td>Level 1 Trauma Centre/Dallas USA</td>
<td>Study</td>
<td>New Jersey Medical School/NJ USA</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>History of brain injury</td>
<td>Coagulopathy including known bleeding disorder or taking warfarin</td>
<td>Immediate neurosurgical intervention including transfer to ICU</td>
<td>Retrospective Cohort Study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outcome measures: Medium risk</td>
<td>No outcome measures after discharge</td>
<td>Confounding Factors: Low risk</td>
<td>No control for poly-trauma and comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical techniques: N/A</td>
<td></td>
<td>Study Recruitment: Low risk</td>
<td>Selection out of lower risk patients that did not have repeat CT imaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confounding Factors: Low risk</td>
<td>No control for poly-trauma and comorbidities</td>
<td>Prognostic factor measurement: low risk</td>
<td>Does not really assess prognostic value of factors measured</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statistical techniques: N/A</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Outcome of CT Imaging

- **50/202 worse CT**
- **5/202 required neurosurgery**, all had persistent or worsening neurology
- **1/202 died** in the persistently abnormal/worsening neurology group
- No clear measure of deterioration
- **Mean/median GCS=14.7**
- **Mean/median age= 44**
- **Percent anticoagulated=0**

### Study Recruitment

- **Low risk**
- Selection out of lower risk patients that did not have repeat CT imaging

### Attrition

- **Low risk**
- Inpatient outcomes

### Prognostic Factor Measurement

- **Low risk**
- Does not really assess prognostic value of factors measured

### Outcome Measures

- **Medium risk**
- No outcome measures after discharge

### Confounding Factors

- **Low risk**
- No control for poly-trauma and comorbidities

### Statistical Techniques

- **N/A**

### Inclusion Criteria

- **Age ≥17**
- **GCS ≥12**
- **TBI with positive initial intracranial CT**

### Study Details

- **341 patients in study (6 patients with bleeds excluded as no F/U scan)**
- **72/341 intubated in ED**
- **105/341 progression on CT**
- **13/341 death 9 due to TBI 4 other causes**
- **12/341 neurosurgical intervention**
- **Mean/median GCS=14.6**
- **Mean/median age= 47**
<table>
<thead>
<tr>
<th>Nasir et al 2011 Karachi Pakistan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specialist Centre Karachi</td>
</tr>
<tr>
<td>Non-probability consecutive sampling</td>
</tr>
</tbody>
</table>

**Inclusion criteria:**
- GCS 14-15
- All ages-15% sample children mean age 36 2 SD 18
- TBI with positive initial CT intracranial injury

**Excluded:**
- Clinical deterioration
- Immediate neurosurgery
- Isolated pneumocephalus

**All patients had a repeat CT within 72 hours**

**Retrospective Cross-sectional study**

**Aim:** Assess the utility of repeat CT scanning in mTBI patients with intracranial injuries without clinical or neurological deterioration

**Worse CT**

**Age**

**Gender**

**Initial GCS**

**Mechanism of injury**

**CT findings**

275 patients met inclusion criteria (note states 255 contusion haematoma)

17/275 worse CT

No patients required neurosurgery

Mean/median GCS = 14.7

Mean/median age = 36

Percent anticoagulated = 0

**Outcome measures: Medium risk**

No outcome measures after discharge

**Confounding Factors: Medium risk**

No control for poly-trauma and comorbidities

**Statistical techniques: N/A**

---

<table>
<thead>
<tr>
<th>Boris et al 2013 Israel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Israel Level 2 trauma centre Sates 2007-2011</td>
</tr>
</tbody>
</table>

**Inclusion criteria:**

**Retrospective Cohort Study**

Assess whether repeat CT imaging in GCS 14-15 mTBI

**Increased size of bleed second CT**

**Clinical deterioration-decrease in GCS**

**Age**

**Sex**

**Initial and follow-up GCS CT findings**

68 patients

4 patients transferred to neurosurgery (2 routine)

8/68 patients worse CT

**Study Recruitment: Medium risk**

Identified on trauma data base with patients with incomplete data excluded. Does not present number of these patients. Also excludes patients transferred

**Attrition: Low Risk**

Low risk- inpatient outcomes

**Prognostic factor measurement: low risk**

Does not really assess prognostic value of factors measured

**Outcome measures: Medium risk**

No outcome measures after discharge

**Confounding Factors: Medium risk**

No control for poly-trauma and comorbidities

**Statistical techniques: N/A**

**Overall**

Includes kids and quite a different population than North America and Europe.
### GCS14-15

TBI with positive initial CT intra-cranial injury including subdural, extra-dural, subarachnoid and intra-cerebral bleeds

Only data for adults presented

Excluded:
- Patients with incomplete data
- Transferred to neurosurgery immediately
- No repeat CT

All patients had a repeat CT within 12 hours

<table>
<thead>
<tr>
<th>Items</th>
<th>New motor or sensory symptoms</th>
<th>12/68 mild deterioration</th>
</tr>
</thead>
<tbody>
<tr>
<td>with intracranial injury justified</td>
<td>Severe headache or vomiting</td>
<td>28 patients intra-parenchymal bleed</td>
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<tr>
<td></td>
<td></td>
<td>1/28 worse CT</td>
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<td></td>
<td></td>
<td>3/28 neurological deterioration</td>
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<td></td>
<td></td>
<td>1/28 transferred to neurosurgery (not patient with worse CT)</td>
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<td></td>
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<td>7 patients extra-dural</td>
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<tr>
<td></td>
<td></td>
<td>1/7 worse CT</td>
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<td></td>
<td></td>
<td>0/7 neurological change</td>
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<tr>
<td></td>
<td></td>
<td>1/7 transferred to neurosurgery</td>
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<tr>
<td></td>
<td></td>
<td>20 patients sub-durals</td>
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<tr>
<td></td>
<td></td>
<td>3/20 worse CT</td>
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<tr>
<td></td>
<td></td>
<td>4/20 neurological deterioration</td>
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<td></td>
<td></td>
<td>1/20 neurosurgery</td>
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<td></td>
<td></td>
<td>13 patients SAH</td>
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<td>3/13 increase in size bleed</td>
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<td></td>
<td></td>
<td>5/13 neurological deterioration</td>
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<td></td>
<td></td>
<td>1/13 transferred to neurosurgery</td>
</tr>
</tbody>
</table>

Mean/median GCS=14.8

Mean/median age= 56

### Brown et al 2007

Los Angeles Level 1 trauma center 2003-2004

Inclusion criteria:
- All patients with blunt head trauma and intra-cranial bleed initial CT. Presents data for GCS13-15

Excluded:
- Immediate neurosurgery
- Died within 24 hours
- Does not state just adults but seems only for adults

Prospective Cohort Study Aim
To identify patients with head injuries that benefit from routine repeat CT imaging

<table>
<thead>
<tr>
<th>Items</th>
<th>Need for neurological intervention- either medical or surgical (medical= sedatives, mannitol or hyperventilation and surgical= ICP monitor and craniotomy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mortality</td>
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<tr>
<td></td>
<td>Age</td>
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<tr>
<td></td>
<td>Gender</td>
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<tr>
<td></td>
<td>Mechanism of Injury</td>
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<tr>
<td></td>
<td>ISS</td>
</tr>
<tr>
<td></td>
<td>Admission GCS</td>
</tr>
<tr>
<td></td>
<td>Results of CT- interpreted by attending radiologist</td>
</tr>
</tbody>
</table>

354 patients all GCS scores with intra-cranial bleed

37 direct to craniotomy

43 dies within 24 hours

274= study population

142/274= mTBI GCS13-15

15/142 had clinical deterioration

27/142 had worse CT scans (only 72/142 had repeat imaging)

5/142 had medical or neurosurgical intervention

3/142 died

Mean/median GCS=14

Mean/median age= 43

Study Recruitment: Mod risk
Removal of patients that died within 24 hours may lead to this sample being a lower risk group than population of interest

Attrition: Low Risk
Low risk- inpatient outcomes

Prognostic factor measurement: low risk
Does not really assess prognostic value of factors measured

Outcome measures: Medium risk
No outcome measures after discharge

Confounding Factors: Medium risk
No control for poly-trauma and comorbidities

Statistical techniques: N/A

### Study Analysis

- **Age**
  - Mean/median GCS=14
  - Mean/median age= 43

- **Gender**
  - Male/Female

- **Mechanism of Injury**
  - blunt head trauma

- **ISS**
  - Injury Severity Score

- **Admission GCS**
  - Glasgow Coma Scale

- **Results of CT- interpreted by attending radiologist**
  - Need for neurological intervention- either medical or surgical (medical= sedatives, mannitol or hyperventilation and surgical= ICP monitor and craniotomy)
<table>
<thead>
<tr>
<th>Inclusion criteria:</th>
<th>Excluded:</th>
<th>Neurosurgical interventions-</th>
<th>Study Recruitment:</th>
<th>Attrition:</th>
<th>Prognostic factor measurement:</th>
<th>Outcome measures:</th>
<th>Confounding Factors:</th>
<th>Statistical techniques:</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients with blunt head trauma and evidence TBI on initial CT.</td>
<td>Penetrating mechanism</td>
<td>craniotomy or ICP monitor</td>
<td>Mod risk</td>
<td>Low Risk</td>
<td>Mod risk</td>
<td>Mod risk</td>
<td>Medium risk</td>
<td>N/A</td>
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<tr>
<td>Present data for GCS13-15</td>
<td>Immediate neurosurgery</td>
<td>Medical interventions- mannitol/hypertonic saline</td>
<td>Dependent on case note review. Patient with “unclear” indications for interventions removed.</td>
<td></td>
<td>Does not explain how CT scans reported</td>
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<td>Age 18+</td>
<td>Interventions for unclear indications</td>
<td>Neurological change-reduced GCS, pupillary change, increased ICP or loss of brain stem reflexes</td>
<td>Only inpatient outcome measures</td>
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<tr>
<td>Died before second CT</td>
<td>All patients repeat CT at 6-8 hours after admission</td>
<td>Interventions for unclear indications</td>
<td>Only inpatient outcome measures</td>
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<td>50 months from Jan 2001</td>
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<td>Mechanism of injury</td>
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<td>Anticoagulant use</td>
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<td>Antiplatelet use</td>
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<td>PT, aPTT, INR</td>
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<td>CT findings</td>
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<td>457/836 in included sample population GCS13-15</td>
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<td>14/457= neurosurgical intervention (craniotomy or ICP bolt)</td>
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<td>3/457 medical management</td>
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<td>5/14 neurosurgical interventions- based on repeat CT</td>
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<td>3/14 medical interventions based on repeat CT</td>
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<td>Mean/median age= 42</td>
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</table>

<table>
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<tr>
<th>Inclusion criteria:</th>
<th>Excluded:</th>
<th>Neurosurgical intervention</th>
<th>Study Recruitment:</th>
<th>Attrition:</th>
<th>Prognostic factor measurement:</th>
<th>Outcome measures:</th>
<th>Confounding Factors:</th>
<th>Statistical techniques:</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS13-15</td>
<td></td>
<td>craniotomy or ICP monitor</td>
<td>Low risk</td>
<td>Low Risk</td>
<td>Mod risk</td>
<td>Low risk</td>
<td>Medium risk</td>
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<tr>
<td>ICD9 code for intra-cranial bleed.</td>
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<td>Medical interventions- mannitol/hypertonic saline</td>
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<td>One hospital transferred all patients to neurosurgical centre.</td>
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<td>Neurological change-reduced GCS, pupillary change, increased ICP or loss of brain stem reflexes</td>
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<td>Other 2 hospitals transferred selected</td>
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<td>Interventions for unclear indications</td>
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<td>Died before second CT</td>
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<td>All patients repeat CT at 6-8 hours after admission</td>
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<td></td>
<td>323 patients all 3 hospital intra-cranial bleed and GCS13-15</td>
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<td>27/323 required neuro-rehab</td>
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<td>2/323 died</td>
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<td>35/323 neurosurgery</td>
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<td>77/323 not transferred- 0/77 died</td>
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<td>0/77 neurosurgery</td>
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<td>2/77 delayed transfer</td>
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<td></td>
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<td>Non-transfer on basis of:</td>
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<td></td>
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<td>Single bleed &lt;= 5mm or contusion &lt;1cm and no coagulopathy</td>
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<td></td>
<td>Mean/median age= 39</td>
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</table>

<table>
<thead>
<tr>
<th>Study Recruitment:</th>
<th>Attrition:</th>
<th>Prognostic factor measurement:</th>
<th>Outcome measures:</th>
<th>Confounding Factors:</th>
<th>Statistical techniques:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mod risk</td>
<td>Low Risk</td>
<td>Mod risk</td>
<td>Mod risk</td>
<td>Medium risk</td>
<td>N/A</td>
</tr>
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<td>Study</td>
<td>Level 1 Trauma Centre New Jersey 2002-2006</td>
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<tr>
<td><strong>Inclusion criteria:</strong></td>
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<tr>
<td>Initial GCS 13-15</td>
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<tr>
<td>Blunt traumatic head injury</td>
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<td>Age 18+</td>
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<tr>
<td>Intra-cranial injury</td>
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<tr>
<td>CT head-ICB or skull fracture</td>
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<tr>
<td>Repeat CT</td>
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<tr>
<td>Abnormal neurological</td>
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<tr>
<td>examination at time of repeat CT</td>
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<td><strong>Excluded:</strong></td>
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<td>Immediate or planned</td>
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<tr>
<td>neurosurgical intervention</td>
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<tr>
<td>Normal neurology</td>
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<td>at time of repeat CT</td>
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<td>normal neurology defined</td>
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<tr>
<td>as GCS15, orientation to</td>
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<td>place, person or time,</td>
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<tr>
<td>normal neurological exam, no</td>
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<tr>
<td>symptoms from head injury-</td>
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<tr>
<td>headache, vomiting, dizziness, lethargy</td>
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<tr>
<td>Coagulopathy</td>
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<td>including known bleeding</td>
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<td>disorder or taking warfarin</td>
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</table>

**Retrospective Cohort Study**

**Aim:** To assess proportion of patients that have worse CT scans and neurosurgical interventions that have abnormal neurology when they have a repeat CT.

**Progression of lesion on CT:** Surgical intervention includes intubation

**Medical intervention:** Persistently Abnormal Neurological exam

**GOSE at discharge:** Unknown whether change as intubated

**Demographics:**

- 107 patients met inclusion criteria
- 63/107 worse CT=59%
- 7/107 neurosurgical group
- 21/107 deterioration
- 18/107 unable to assess neurology as intubated.
- 6 died

- Mean/median GCS=14.4
- Mean/median age= 48
- Percent anticoagulated=0

**Statistical techniques:** N/A

None done

**Study Recruitment:** High risk

High risk subgroup that have abnormal neurology at time of repeat CT imaging.

**Attrition:** Low Risk

Only inpatient outcome measures

**Prognostic factor measurement:** Mod risk

Difficult to assess deterioration in a retrospective study.

**Outcome measures:** Mod risk

No F/U after discharge

**Confounding Factors:** Low risk

Some control for comorbidities.

**Statistical techniques:** N/A

None done
### Supplementary Material 2: Data Extracted from Included Studies

#### Studies Only Included in Meta-Analysis of Prevalence of Outcomes N=26

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Study Design</th>
<th>Outcome Measures</th>
<th>Prognostic factors assessed</th>
<th>Results</th>
<th>Quality Appraisal</th>
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<tbody>
<tr>
<td>Nishijima et al 2013</td>
<td>Sacramento, USA</td>
<td>Multicenter, 8 sites</td>
<td>Retrospective Cohort Study</td>
<td>Initial ICU admission from ED</td>
<td>Age, Initial GCS, Initial BP</td>
<td>11240 patients coded as bleeds</td>
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<td></td>
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<td></td>
<td></td>
<td>771 excluded due to missing data</td>
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<tr>
<td>Beynon et al 2015</td>
<td>Heidelberg University Hospital, Germany</td>
<td>Retrospective Cohort Study</td>
<td>Repeat CT imaging</td>
<td>Prognostic factors assessed</td>
<td>74 patients met inclusion criteria. 37 no anticoagulation</td>
<td>Study Recruitment: Low risk</td>
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<td>37 anticoagulated, 37 in no anticoagulation group</td>
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<td>Significant variation between sites</td>
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<td>Note initial GCS 15- lower risk group</td>
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<td>Follow up only during hospital admission</td>
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<td>Follow up only during hospital admission</td>
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<td>No F/U after discharge</td>
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<td>No control for comorbidities.</td>
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<td></td>
<td>Statistical techniques: N/A</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>None done</td>
</tr>
</tbody>
</table>
with minor traumatic intracranial haemorrhages

- Age > 18 years
- Traumatic ICH
- Initial ED GCS 15
- ISS less than 16

multiple trauma centres. Invasive monitoring

2) Estimate the proportion of minor traumatic intracranial haemorrhages patients admitted to ICU that do not receive an ICU intervention

847/888 patients admitted ICU no crit care intervention

Mean/median GCS=15
Mean/median age=48

Prognostic factor measurement: Low risk

Outcome measures: Low risk

Doesn’t really apply as testing disposition not outcomes

Confounding Factors:

Study Recruitment: Mod risk bias
Dependent on accuracy on recording on trauma registry and accuracy of case notes.

Low risk group- GCS 15 and benign CT

Attrition: Low risk
Loss of 37 patients to follow up

Prognostic factor measurement: Low risk

As recorded in case notes so dependent on accuracy

Outcome measures: Low risk

As recorded in case notes so dependent on accuracy

Confounding Factors:

Patients which are perceived as higher risk will be put on ICU, likely to be differences in comorbidities

Statistical techniques: low risk

Well presented- not really relevant to meta-
Schaler et al 2015
Level 1 Trauma centre
Bern Switzerland
Jan 2006-Dec 2007

Inclusion criteria:
- Admission GCS 13-15
- Observed for 24H
- Localised intracranial bleeds up to 5mm - this is from the CCHR paper

Exclusion Criteria:
- Bleeds > 5mm maximum diameter
- Multiple bleeds
- History of bleeding tendency
- Anti-coagulant or anti-platelet medication
- Intoxication
- Other injuries
- Live alone
- Live greater than 1H from hospital

Retrospective cohort study/case series
Aim to assess if a specific group of patients with small bleeds can be discharged from hospital without 24 hours of observation
Deterioration in neurological status or need for neurosurgery.

Prognostic factors are the inclusion/exclusion criteria
No comparison in risk of deterioration in 2 groups.

110 patients met inclusion and exclusion criteria.
None deteriorated within the period of hospital observation, required neurosurgery or re-attended.
Mean/median GCS=14.6
Mean/median age= 40
Percent anticoagulated=0

Study Recruitment: Low risk bias
Retrospective cohort review- reliant on accuracy of written notes.

Attrition: Mod risk
Patients may have moved out of catchment area of hospital without the researchers being aware. Loss to F/U if re-presented at different hospital.

Prognostic factor measurement: Mod risk
Reliability of case notes- may be incomplete Interpretation size of the bleed was taken from written radiology report ?reliability.

Outcome measures: Moderate risk
Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration. Not clear how patients died in the community would have been identified.

Confounding Factors: Low risk
No obvious confounding factors
Cohort selection criteria including not living alone may select out high risk older patients.

Statistical techniques: N/A

General comments:
Mean age 39.9 years and 25% caused by sporting injuries. ?Age as the confounding low risk prognostic factor. Not generalizable to older populations

Small numbers
<table>
<thead>
<tr>
<th>Study Recruitment: Low risk bias</th>
<th>Patients recruited from trauma registry depends on how good this is</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Only admitted patients: higher acuity patients then discharged.</td>
</tr>
<tr>
<td></td>
<td>Likely patients admitted for other reasons if CT negative TBI (although excludes other injuries).</td>
</tr>
<tr>
<td>Attrition: Low risk</td>
<td>All inpatient outcomes</td>
</tr>
<tr>
<td>Prognostic factor measurement: Mod risk</td>
<td>CT findings abstracted from CT reports- severity assigned by language- not actually used in regression model</td>
</tr>
<tr>
<td>Outcome measures: Moderate risk</td>
<td>Only inpatient outcomes- possibility of discharge and deterioration</td>
</tr>
<tr>
<td>Confounding Factors: High risk</td>
<td>Patients admitted with CT negative TBI likely to be frail or have other reasons for admission- this will affect outcome measures compared to SAH patients admitted due to +ve CT.</td>
</tr>
<tr>
<td>Statistical techniques: Low risk</td>
<td>Well presented.</td>
</tr>
<tr>
<td>Can use for pooling for outcomes SAH-supports low risk sub-population</td>
<td></td>
</tr>
<tr>
<td>Inclusion criteria:</td>
<td>Length of stay</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Admission GCS 13-15</td>
<td>Mortality</td>
</tr>
<tr>
<td>CT positive intra-cranial injury</td>
<td></td>
</tr>
<tr>
<td>Not transferred to neurosurgical unit in accordance with non-transfer policy</td>
<td></td>
</tr>
<tr>
<td>CT findings of small SAH</td>
<td></td>
</tr>
<tr>
<td>Punctate or minimal contusion</td>
<td></td>
</tr>
<tr>
<td>Punctate or minimal intra-cranial bleed</td>
<td></td>
</tr>
<tr>
<td>Small SDH, no mass effect</td>
<td></td>
</tr>
</tbody>
</table>

Exclusion Criteria:
- Any coagulopathy
- Basilar skull fracture or evidence of CSF leak
- Extra-dural bleed
- Any significant contusion or SDH/intra-cerebral haemorrhage

**Review and discussion of CT and patient with neurosurgeon if unsure if should be transferred**

76/273 patients not transferred
>50% injuries due to skiing/snowboarding
71% patients less than 55

No patient deteriorated, died or required neurosurgery or required delayed transfer whilst admitted to hospital.

2 patients re-admitted within 90 days - 1 patient 6 weeks following admission developed an acute on chronic subdural- drained. 1 patient re-admitted with unrelated complaint.

Mean/median GCS=14.7
Mean/median age= 36
Percent anticoagulated=0

**Study Recruitment:** Low risk bias
Retrospective cohort review- reliant on accuracy of written notes. CT inclusion criteria are subject and patients may have been transferred despite meeting non-transfer policy if clinicians were concerned.

**Attrition:** Low risk
Prognostic factor measurement: Mod risk Reliability of case notes- may be incomplete. The definitions of bleed size are subjective.

**Prognostic Factors**
N/A

**Outcome measures:** Moderate risk
Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration.

**Confounding Factors:** Low risk
Age affect outcome and size of bleed

**Statistical techniques:** N/A

**General points**
Small numbers. No comparator group- need to compare to transferred patients outcomes.

Patient not generalizable- v. young and atypical mechanism of injury (mostly winter sports related).

Likely that any patient clinicians felt risky would have been transferred even if did not meet transfer criteria- no way to check this.
| Joseph et al  
USA  
2013  
The acute care surgery model: Managing traumatic brain injury without an inpatient neurosurgical consultation.  
| Inclusion criteria:  
• GCS13-15  
• Trauma  
• Positive findings  
CT- skull fracture and/or ICH  
| Exclusion Criteria:  
• Pre-hospital anti-platelets or anti-coagulants  

| Retrospective cohort study- propensity matching 1:2 ratio patients managed solely by trauma surgeons versus patients that had neurosurgical consultation.  
Hypothesis  
Trauma surgeons can manage mTBI patients with CT detected intracranial haemorrhage without neurosurgical involvement.  
| Hospital admissions  
ICU admissions  
Neurosurgical interventions  
ED visits after discharge  
Mortality  
Progression on CT imaging  
| Age  
Sex  
Initial GCS  
ISS  
Head-abbreviated injury score  
Neurological examination  
CT scan findings-type of skull fracture/type of ICH/size of bleed-reviewed by study investigator  
| 404-GCS13-15 patients with CT detected injuries in study period.  
270/404 used for this study  
90/270- had neurosurgical consultations (NC)  
180 no neurosurgical consultation. (no-NC)  
Whether neurosurgical consultation requested as discretion of non-specialist surgeon. Propensity matching in this study between 2 groups.  
0/270 neurosurgical interventions, hospital mortality or readmissions either group.  
78/90 no-NC and 158/180 NC admitted hospital (P=0.8)  
18/90 no-NC and 80/180 NC admitted ICU (P=0.001)  
Routine repeat CT 18/90 no-NC 155/180 NC (P<0.001)  
No progression on any repeat CT  
8% no-NC and 4% NC group re-attended ED. No readmissions.  
Mean/median GCS=15  
Mean/median age= 30  

| Study Recruitment: High risk bias  
Subset of patients that meet inclusion criteria selected in order to facilitate propensity matching. Possible selection out of higher acuity patients as these will have al been referred to a neurosurgeon.  
Attition: low risk  
In patient outcomes and documented ED re-attendances- low risk of patients being lost to follow up  
Prognostic factor measurement: Low risk  
All routinely collected clinical data apart from CT imaging which re-reviewed.  
Outcome measures: Mod risk  
Study dependent on patients re-presenting at the same hospital following discharge if had delayed deterioration.  
Confounding Factors: Mod risk  
Does not exclude patients with additional injuries  

Mean/median GCS=15  
Mean/median age= 30
<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Study Recruitment</th>
<th>Attrition</th>
<th>Prognostic factor measurement</th>
<th>Outcome measures</th>
<th>Statistical techniques</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbdelFattah et al 2012</td>
<td>Level 1 trauma center Dallas Texas</td>
<td>Prospective recruitment 2010-2011</td>
<td>Low risk</td>
<td>Low risk</td>
<td>Neurologic progression</td>
<td>Hypothesis: Repeat CT imaging in GCS13-15 with ICH, without neurological progression, does not impact the need for neurosurgical intervention.</td>
<td>High risk</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td>Medical intervention</td>
<td>Outcome measures during hospital admission: Age, Sex, Coagulation status, Neurosurgical intervention</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repeat CT imaging: worse CT defined as worse by a blinded radiologist/neurosurgeon giving qualitative measure of bleed.</td>
<td></td>
<td>Small numbers.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Comparison between groups: Age, Sex, Coagulation status, Neurosurgical intervention</td>
<td></td>
<td>Likely reporting data reported elsewhere.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>145 patients met inclusion/exclusion criteria.</td>
<td>92/145 for routine repeat CT, 53/145 for CT if deteriorated</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Otherwise groups comparable</td>
<td>5/53 deteriorated and had a repeat CT + 1/53 had repeat scan as started on warfarin</td>
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<td></td>
<td>1/145 patients died (due to other injuries)</td>
<td>27/145 radiological deterioration, 9/145 patients intubated: states for other injuries</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Mean/median GCS=14.5</td>
<td>Mean/median age=41</td>
<td>Percent anticoagulated=6</td>
</tr>
<tr>
<td>Nayak et al 2013</td>
<td>University Hospital Newark New Jersey</td>
<td>Retrospective Chart Review 2003-2008</td>
<td>Low risk</td>
<td>Mod risk</td>
<td>Age, Sex, Mechanism of Injury</td>
<td>Retrospective case note review- depends on information being recorded correctly</td>
<td>Low risk</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td>Neurosurgical intervention after 24 hours- craniotomy, ventriculostomy, ICP bolt/measurement</td>
<td>321/864 patients GCS13-15 with ICB met inclusion criteria</td>
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<tr>
<td></td>
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<td></td>
<td>Death in hospital</td>
<td>20% excluded because incomplete medical notes/transfers</td>
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<td></td>
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<td></td>
<td>Discharge disposition</td>
<td>0/321 neurosurgical intervention-all within 24 hours of admission</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Age, Sex, Mechanism of Injury</td>
<td>No deaths</td>
<td>Study Recruitment: Low risk</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>Neurosurgical intervention after 24 hours- craniotomy, ventriculostomy, ICP bolt/measurement</td>
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<td>Age, Sex, Mechanism of Injury</td>
<td>No deaths</td>
<td>Study Recruitment: Low risk</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Age, Sex, Mechanism of Injury</td>
<td>No deaths</td>
<td>Study Recruitment: Low risk</td>
</tr>
</tbody>
</table>

Additional notes:
- Small study with confounders regarding outcomes.
- Statistical techniques: Low risk
- None
- Study Recruitment: Low risk
- Prospective recruitment - states recruited all eligible patients. Doesn't explain how recruitment occurred.
- Attrition: Low risk
- Follow up only for period in hospital
- Prognostic factor measurement: Low risk
- Blinded appraisal of CT scans by researcher.
- Outcome measures: Mod risk
- No F/U following discharge- missed delayed outcomes, could have looked for re-attendance. Doesn't report neurosurgical outcome measures.
- Confounding Factors: High risk
- Not isolated head injury- other injuries have clearly affected outcome measures
- Statistical techniques: Low risk
- None
- Small study with confounders regarding outcomes
- Study Recruitment: Low risk
- Retrospective case note review- depends on information being recorded correctly
- Attrition: Mod risk
- 20% excluded because of incomplete notes
- Prognostic factor measurement: Mod risk
### Anandalwar et al. 2016

**University Hospital Newark New Jersey**  
Level 1 trauma centre 2009-2012

#### Inclusion criteria:
- Aged 18 and over  
- Blunt trauma  
- Intra-cranial bleed/skull fracture  
- Admitted to hospital

| Neurological examination managed with and without a repeat CT head scan | LOS hospital | Neurological examination every 2 hours- routine care on a flow sheet | 19/142 worse CT on repeat CT after 24 hours of admission  
179/321 single CT  
142/321 routine repeat CT  
76/321 returned to F/U clinic- uneventful  
14/321 returned to ED due to symptoms.  
Mean/median GCS=14.9 Mean/median age= 41

#### Retrospective cohort study

**Aim**
Assess the outcomes following the implementation of a policy of observation only (no repeat CT imaging) for GCS 15 patients

**Repeat CT after 24 hours of admission due to clinical concern or deterioration.**  
Progression on any repeat CT completed.  
Neurosurgical interventions.  
Intubation, ICU admissions, administration of mannitol.  
ED revisits within 1 year for  
533 patients TBI and ICH  
142 met the inclusion/exclusion criteria  
47 underwent a routine repeat CT within 24 hours (violation of policy); 0/47 neurosurgical  
1/47 had incidental finding on CT  
95 no repeat routine CT within 24 hours  
8/95 (non-violation group) had repeat CT >24 hours after admission- due to concern.  
3/8 progression on CT

#### Study Recruitment: High risk  
 Patients at GCS15 at 24 hours- low risk group selected out- difficult to extrapolated to all GCS 13-15 patients.  
Does not compare outcomes in patient that adhered to and violated non-routine repeat CT head imaging. Potentially clinicians ordered routine repeat CT imaging on riskier patients.

#### Attrition: Low Risk  
Potential for patients to have re-attended
### Ditty et al. 2015

**University Alabama Level 1 trauma centre**
**2003-2013**

**Inclusion criteria:**
- 500 consecutive patients present on trauma registry
- GCS13-15
- ICD9 diagnosis SAH and/or intraparenchymal contusion-confirmed with Retrospective Cohort Study

**Aim**
Assess the clinical implications of SAH or intraparenchymal haemorrhage in mTBI

<table>
<thead>
<tr>
<th>GCS13-15 on arrival to ED</th>
<th>GCS 15 24 hours after attendance to ED</th>
<th>Did not receive a repeat CT head scan</th>
<th>Excluded:</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of neurological or psychiatric disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate neurosurgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous TBI or neurosurgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete notes</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients that did undergo a repeat CT scan despite meeting the rest of inclusion/exclusion criteria formed a comparison group.

**TBI related symptoms.**

**1 neurosurgical intervention**

2/8 admitted to ICU due to deterioration- 1 intubated

3/95 patients returned with 1 year to the ED due to TBI symptoms- all underwent repeat CT. No admissions.

Mean/median GCS=14.8
Mean/median age= 38
Percent anticoagulated=0

**Outcome measures:**
- Low risk
- Delayed neurosurgical evacuation as inpatient.
- Neurological decline- altered mental state or focal neurological deficit.
- Inpatient mortality.
- Admission GCS
- Anti-coagulation
- Anti-platelets
- Transfer Distances
- Sex
- Age
- Haemorrhage type

500 patients met inclusion criteria

| 411/500 isolated SAH |
| 63/500 isolated ICH |
| 26/500 both |

463 GCS15
30 GCS14
8 GCS13

469/500 patients pre-hospital medication available (71/469 taking either anti-coagulants or anti-platelets)

156/500 transfers

**Study Recruitment:**
- Mod risk
  - High proportion of transferred patients may represent higher or lower acuity patients than general population.

  - Higher as being transferred to specialist centre, lower as survived /fit to transfer.

**Attrition:**
- Low Risk
  - Only inpatient measures

**Confounding Factors:**
- Mod risk
  - No details about inclusion or completeness of trauma registry.

**Prognostic factor measurement:**
- Low risk
  - No risk model developed

**Statistical techniques:**
- Low risk
  - None presented

Is a lower risk population due to selection for repeat CT imaging and return to GCS15 at 24 hours- possibly unable to include in any meta-analysis.

<table>
<thead>
<tr>
<th>Ditty et al. 2015</th>
<th>University Alabama Level 1 trauma centre 2003-2013</th>
<th>Inclusion criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiology report and neurosurgical consult note: if disagreement scan re-reviewed if not clear patient excluded</td>
<td>Clinical deterioration (defined as decrease in mental status, worsening neurologic exam or death) Neurosurgery during admission Progression on CT.</td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>Excluded:</td>
<td>No patients had seizures. No patients had neurological decline. No patients underwent delayed neurosurgical intervention. No inpatient mortality</td>
<td></td>
</tr>
<tr>
<td>Diagnoses extra or subdural hematoma</td>
<td>Prognostic factor measurement: Mod risk</td>
<td></td>
</tr>
<tr>
<td>Penetrating injuries</td>
<td>Incomplete information regarding medications.</td>
<td></td>
</tr>
<tr>
<td>Fatal extra-cranial injuries</td>
<td>May be other inaccurate recording of factors.</td>
<td></td>
</tr>
<tr>
<td>CSF leak</td>
<td>Outcome measures: Mod risk</td>
<td></td>
</tr>
<tr>
<td>Aneurysmal SAH</td>
<td>Only inpatient related outcome measures.</td>
<td></td>
</tr>
<tr>
<td>Delayed presentation</td>
<td>Confounding Factors: Mod risk</td>
<td></td>
</tr>
<tr>
<td>Pruitt et al 2016 Chicago USA</td>
<td>Cohort includes patients with multiple injuries- only excluded if died from other injuries.</td>
<td></td>
</tr>
</tbody>
</table>

#### Prudit et al 2016 Chicago USA

**Level 1 Trauma Centre Chicago 2009-2013**

**Inclusion criteria:**
- Initial GCS13-15
- 16 and older
- Traumatic intra-cranial bleed or skull fracture
- Identified on electronic ED system using ICD 9 classification system
- Admitted to ED observation unit

All patients received a neurosurgical consultation

<table>
<thead>
<tr>
<th>Retrospective cohort study</th>
<th>Clinical deterioration (defined as decrease in mental status, worsening neurologic exam or death) Neurosurgery during admission Progression on CT.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aim</strong></td>
<td>Age Gender Method of arrival Whether transfer Comorbidities Anticoagulant use Mechanism of injury Initial GCS, Neurological examination Alcohol intoxication Initial platelet count INR Initial CT results Follow-up CT results, Neurosurgical recommendations Cranial CT data were collected from attending radiologist</td>
</tr>
<tr>
<td></td>
<td>1185 GCS13-15 with CT detected injuries</td>
</tr>
<tr>
<td></td>
<td>814 admitted directly to hospital- poly-trauma, social reasons or as neurosurgeons felt high risk.</td>
</tr>
<tr>
<td></td>
<td>371 left under care of ED. Of these, 239/371 transferred ED obs unit. 132/371 discharged directly from the ED after a period of observation.</td>
</tr>
<tr>
<td>Admitted patients</td>
<td>Study Recruitment: High risk</td>
</tr>
<tr>
<td></td>
<td>Neurosurgeons have admitted higher risk patients we can combine outcomes from both admitted and ED observed patients to give an unbiased estimate.</td>
</tr>
<tr>
<td></td>
<td>Attrition: Med Risk</td>
</tr>
<tr>
<td></td>
<td>Only a proportion of patients are followed up- does not describe the mechanism for this or how consistent follow up is e.g. did they all get repeat CT scans</td>
</tr>
<tr>
<td></td>
<td>Prognostic factor measurement: Medium risk</td>
</tr>
<tr>
<td></td>
<td>Dependent on CT scan reports and written documentation</td>
</tr>
<tr>
<td></td>
<td>Outcome measures: Mod risk</td>
</tr>
<tr>
<td></td>
<td>Clinical deterioration not well defined and very broad.</td>
</tr>
<tr>
<td></td>
<td>Confounding Factors: Low risk</td>
</tr>
</tbody>
</table>

**Study Recruitment:** High risk

Neurosurgeons have admitted higher risk patients we can combine outcomes from both admitted and ED observed patients to give an unbiased estimate.

**Attrition:** Medium risk

Only a proportion of patients are followed up—does not describe the mechanism for this or how consistent follow up is e.g. did they all get repeat CT scans

**Prognostic factor measurement:** Medium risk

Dependent on CT scan reports and written documentation

**Outcome measures:** Mod risk

Clinical deterioration not well defined and very broad.

**Confounding Factors:** Low risk
Deepika et al. 2013
Bangalore India

Patients admitted tertiary neurosurgical centre 3 months Jan-Mar 2010. Patients identified on a TBI registry

Inclusion criteria:
- GCS 13-15 head injury
- Underwent CT scan
- Either negative CT or isolated traumatic subarachnoid
- Matched comparison between patients - ve CT and SAH

Excluded:
- Does not state adults only but age

| Retrospective cohort study | Prospective 1 year telephone assessment of: GOSE Rivermead post concussion questionnaire Rivermead Head injury follow up questionnaire | Age Sex Mechanism of injury RTC Fall LOC Seizure Location of SAH Whether multiple bleeds Thickness greater or less than 5mm | 34/1628 mTBI patients isolated traumatic subarachnoid haemorrhage
18/34 patients available for follow up at 1 year Good GOSE Rivermead scores comparable to 16 normal CT controls |

| reports- type and size of detected injury | Concussive symptoms 16/239 Discharged ED Follow up 111/132 Delayed Neurosurgery 111/132 Post traumatic seizure 2/132 Concussive symptoms 8/132 |

Figures from table- author has confirmed this is correct: 155 Isolate SAH 0 no clinical or radiological deterioration or cases of neurosurgery. 161 SDH- 6 CT deterioration, 3 planned neurosurgical outcomes. 0 deteriorated clinically 1 neurosurgery greater then 3 weeks later following outpatient assessment. 30 contusion 5 worsening CT scans. Nil clinical deterioration or emergency neurosurgery. 5 extradural- nil deterioration or neurosurgery |

Of sample 1053 mean/median age=59 11% anticoagulated. Of sample 1185 mean median age=59 10% anticoagulated Included patients with polytrauma and significant comorbidities

Statistical techniques: High Risk
None presented but data presented in table and text do not match up Paper shows patients admitted to hospital by neurosurgeons have worse outcomes/more likely to require neurosurgery.

Does show that in America some of this patient population discharged directly from ED. Consistent with the model used locally in Hull.

Study Recruitment: Low risk
Cohort identified in TBI registry which is part of normal practice. Is retrospective so limited by accuracy of medical notes.

Attrition: High Risk
Small sample- with large proportion lost to followup.

Prognostic factor measurement: Medium risk
Dependent on CT scan reports and written documentation

Outcome measures: High risk
1 year too long

Confounding Factors: Medium risk
No control for other injuries or comorbidities

Statistical techniques: N/A
<table>
<thead>
<tr>
<th>Study Title</th>
<th>Level trauma center</th>
<th>Study Recruitment</th>
<th>Attrition</th>
<th>Prognostic factor measurement</th>
<th>Outcome measures</th>
<th>Confounding Factors</th>
<th>Statistical techniques</th>
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</thead>
<tbody>
<tr>
<td>Kreitzer et al 2014 Cincinnati USA</td>
<td>Level trauma center 2001-2010 Identified from cohort of patients undergone 2 CT within the ED within 24 hours</td>
<td>Retrospective cohort study</td>
<td>Low risk</td>
<td>Medium risk</td>
<td>Low risk</td>
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<td>Study</td>
<td>Institution</td>
<td>Date</td>
<td>Study Design</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Study Aim</td>
<td>Neurosurgical Intervention</td>
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<td>Ding et al 2012</td>
<td>Neurosurgical Centre China</td>
<td>2009-2010</td>
<td>Randomized control trial</td>
<td>All patients with TBI with evidence of intra-cranial haemorrhage - some data for GCS 13-15</td>
<td>Immediate neurosurgery</td>
<td>To assess the need for CT scans following routine CT in patients with traumatic TBI and evidence of intra-cranial haemorrhage</td>
<td>GCS at discharge Surgical and medical interventions secondary to CT</td>
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<tr>
<td>Huynh et al 2006</td>
<td>Level 1 trauma centre USA</td>
<td>2004-2005</td>
<td>Retrospective cohort study</td>
<td>mTBI Blunt trauma to head GCS 15 Abnormal CT head</td>
<td>Normal initial CT head Length of admission less than 48 hours Age less than 18</td>
<td>To assess whether neurosurgical review is necessary in GCS 15 patients with intra-cranial injuries</td>
<td>Changes on follow up CT all patients had routine repeat CT</td>
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<tr>
<td>Study</td>
<td>Neuroneurosurgical centre</td>
<td>Retrospective cohort study + meta-analysis to assess whether repeat CT imaging necessary in mTBI with intra-cranial haemorrhage</td>
<td>Intervention including:</td>
<td>Demographics</td>
<td>Study Recruitment:</td>
<td>Study Recruitment:</td>
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<tr>
<td>Almenawer et al 2013</td>
<td>Neurosurgical centre</td>
<td>To assess whether repeat CT imaging necessary in mTBI with intra-cranial haemorrhage</td>
<td>Mannitol or hypertonic saline, surgical intervention including ICP bolt or craniotomy</td>
<td>GCS 13-15, ISS</td>
<td>High risk</td>
<td>High risk</td>
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<tr>
<td>Ontario, Canada</td>
<td></td>
<td>Neurological changes: decrease GCS, cranial nerve change, vomiting and headache</td>
<td></td>
<td>1121 patients with mTBI and ICH</td>
<td>121 patients met inclusion criteria</td>
<td>Dependent on accuracy of trauma database</td>
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<td>2006-2011</td>
<td>Identified from trauma database</td>
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<td>91/445 worse CT</td>
<td>91/445 worse CT</td>
<td>Large proportion of mTBI patients with ICH did not meet inclusion criteria- selection out of higher risk patients that did not undergo repeat imaging</td>
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<tr>
<td>Inclusion criteria:</td>
<td>GCS 13-15</td>
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<td>21/445 patients neurosurgical outcomes (all preceded by clinical deterioration prior to repeat CT)</td>
<td>21/445 patients neurosurgical outcomes (all preceded by clinical deterioration prior to repeat CT)</td>
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<td></td>
<td>Blunt traumatic head injury</td>
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<td>4/445 patients medical intervention</td>
<td>4/445 patients medical intervention</td>
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<td>Age&gt;17</td>
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<td>2/4 medical outcomes= treated with mannitol due solely worse CT other 2 treated due to clinical deterioration.</td>
<td>2/4 medical outcomes= treated with mannitol due solely worse CT other 2 treated due to clinical deterioration.</td>
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<td>Intra-cranial injury</td>
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<td>Mean/median GCS=14.5</td>
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<td>CT head</td>
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<td>Mean/median age=45</td>
<td>Mean/median age=45</td>
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<td>Repeat CT scan</td>
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<td>Percent anticoagulated=0</td>
<td>Percent anticoagulated=0</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td></td>
<td>No repeat CT scan</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td>Previous craniotomy</td>
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<td>Low risk- inpatient outcomes</td>
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<td>Cranial pathology</td>
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<td>Low risk- inpatient outcomes</td>
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<td>Immediate Neurosurgery</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td>Patients divided into</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td>those underwent intervention due to clinical deterioration or due to repeat CT findings</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td>Inpatient neurological deterioration- abnormal neurology- confusion, disorientation or drowsiness</td>
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<td>Inpatient neurosurgical interventions</td>
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<td>Sifri et al 2004</td>
<td>Level Trauma Centre</td>
<td>To assess the value of routine repeat CT imaging in mTBI patients with intra-cranial haemorrhage</td>
<td>CT results as abstracted from radiologist and neurosurgeons reports.</td>
<td>GCS 14-15, ISS</td>
<td>Medium risk</td>
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<td>USA</td>
<td>New Jersey</td>
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<td>Best ED GCS Demographics</td>
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<td>1999-2001</td>
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<td>243 patients with mTBI and ICH</td>
<td>243 patients with mTBI and ICH</td>
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<td>Inclusion criteria:</td>
<td>GCS 14-15</td>
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<td>18/243 excluded as no repeat CT- neurosurgeon ruled insignificant lesion</td>
<td>18/243 excluded as no repeat CT- neurosurgeon ruled insignificant lesion</td>
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<td>Blunt traumatic head injury</td>
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<td>202/243 included as met the rest of inclusion criteria</td>
<td>202/243 included as met the rest of inclusion criteria</td>
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<td>Age&gt;15</td>
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<td>At 24 hours:</td>
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<td>Intra-cranial injury</td>
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<td>151/202 persistently normal or improving neurology</td>
<td>151/202 persistently normal or improving neurology</td>
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<td>CT head</td>
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<td>51/202 persistently abnormal or worsening neurological examination</td>
<td>51/202 persistently abnormal or worsening neurological examination</td>
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<td>Repeat CT</td>
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<td>50/202 worse CT</td>
<td>50/202 worse CT</td>
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<td>Low risk</td>
<td>Low risk- inpatient outcomes</td>
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<td>History of brain injury</td>
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<td>Population</td>
<td>Outcome Measures</td>
<td>Confounding Factors</td>
<td>Statistical Techniques</td>
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<td>Phelan et al 2014 Dallas USA</td>
<td>Level 1 Trauma Centre Dallas Texas 2010-2012</td>
<td>Patients identified on TBI data base Inclusion criteria: - Intracranial haemorrhage - TBI - Patients divided into SAH and non SAH bleed All GCS but data for GCS13-15 patients presented</td>
<td>Excluded: - Ages less than 18 - Pregnant - Prisoners</td>
<td>Retrospective Cohort Study Assess whether outcomes for mTBI with isolated traumatic subarachnoid differ for other kinds of intra-cranial bleeds</td>
<td>Worse repeat CT imaging if any Death Craniotomy</td>
<td>CT findings as reread by a study team member Age ISS HAS Emergency department GCS</td>
<td>5/202 required neurosurgery- all had persistent or worsening neurology 1/202 died all in the persistently abnormal/worsening neurology group No clear measure of deterioration Mean/median GCS=14.7 Mean/median age= 44 Percent anticoagulated=0</td>
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<tr>
<td>Homnick et al 2012 New Jersey USA</td>
<td>New Jersey Medical School Level 1 trauma centre 2002-2005</td>
<td>Inclusion criteria: - Age&gt;17 - GCS&gt;12 - TBI with positive initial CT-intracerebral bleed, contusion, subdural, extra-</td>
<td>Neurosurgical intervention Progression on CT-repeat CTS as discretion of neurosurgeon Age Sec Pre-injury anticoagulation Mechanism ISS Initial GCS</td>
<td>Retrospective Cohort Study Establish how long intra-cranial bleeds in mTBI continue to expand</td>
<td>Age Sec Pre-injury anticoagulation Mechanism ISS Initial GCS</td>
<td>341 patients in study (85 mTBI patients with bleeds excluded as no F/U scan) 72/341 intubated in ED 105/341 progression on CT 13/341 death- 9 due to TBI 4 other causes 12/341 neurosurgical intervention</td>
<td>Study Recruitment: Low risk Dependent on accuracy of trauma registry Attrition: Low Risk Low risk- inpatient outcomes Prognostic factor measurement: low risk Does not really assess prognostic value of factors measured Outcome measures: Medium risk No outcome measures after discharge Confounding Factors: Low risk No control for poly-trauma and comorbidities Statistical techniques: N/A</td>
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</table>
**Inclusion criteria:**
- GCS 14-15
- All ages -15%
- Sample children mean age 36 ± SD 18
- TBI with positive initial CT intracranial injury

**Excluded:**
- Clinical deterioration
- Immediate neurosurgery
- Isolated pneumocephalus

All patients had a repeat CT within 72 hours

**Aim:** Assess the utility of repeat CT scanning in mTBI patients with intracranial injuries without clinical or neurological deterioration

**Worse CT**
- Age
- Gender
- Initial GCS
- Mechanism of injury
- CT findings

275 patients met inclusion criteria (note states 255 contusion haematoma)

17/275 worse CT

No patients required neurosurgery

Mean/median GCS=14.7
Mean/median age= 36
Percent anticoagulated=0

**Confounding Factors:** Medium risk
No control for poly-trauma and comorbidities

**Statistical techniques:** N/A

**Study Recruitment:** Medium risk
Does not adequately define deterioration or over what period

**Attrition:** Low Risk
Low risk - inpatient outcomes

**Prognostic factor measurement:** low risk
Does not really assess prognostic value of factors measured

**Outcome measures:** Medium risk
No outcome measures after discharge

**Confounding Factors:** Medium risk
No control for poly-trauma and comorbidities

**Statistical techniques:** N/A

**Overall**
Includes kids and quite a different population than North America and Europe.
<table>
<thead>
<tr>
<th>Initial CT intra-cranial injury including subdural, extra-dural, subarachnoid and intra-cerebral bleeds</th>
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<tbody>
<tr>
<td>• Only data for adults presented</td>
</tr>
<tr>
<td>• Patients with incomplete data</td>
</tr>
<tr>
<td>• Transferred to neurosurgery immediately</td>
</tr>
<tr>
<td>• No repeat CT</td>
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<tr>
<td>All patients had a repeat CT within 12 hours</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe headache or vomiting</th>
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<tbody>
<tr>
<td>28 patients intra-parenchymal bleed</td>
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<tr>
<td>1/28 worse CT</td>
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<tr>
<td>3/28 neurological deterioration</td>
</tr>
<tr>
<td>1/28 transferred to neurosurgery (not patient with worse CT)</td>
</tr>
<tr>
<td>7 patients extra-dural</td>
</tr>
<tr>
<td>1/7 worse CT</td>
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<tr>
<td>0/7 neurological change</td>
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<tr>
<td>1/7 transferred to neurosurgery</td>
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<tr>
<td>20 patients sub-durals</td>
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<tr>
<td>3/20 worse CT</td>
</tr>
<tr>
<td>4/20 neurological deterioration</td>
</tr>
<tr>
<td>1/20 neurosurgery</td>
</tr>
<tr>
<td>13 patients SAH</td>
</tr>
<tr>
<td>3/13 increase in size bleed</td>
</tr>
<tr>
<td>5/13 neurological deterioration</td>
</tr>
<tr>
<td>1/13 transferred to neurosurgery</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Attrition: Low Risk</th>
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</thead>
<tbody>
<tr>
<td>Low risk- inpatient outcomes</td>
</tr>
<tr>
<td>Prognostic factor measurement: low risk</td>
</tr>
<tr>
<td>Does not really assess prognostic value of factors measured</td>
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<tr>
<td>Outcome measures: Medium risk</td>
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<tr>
<td>No outcome measures after discharge</td>
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<tr>
<td>Confounding Factors: Medium risk</td>
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<tr>
<td>No control for poly-trauma and comorbidites-</td>
</tr>
<tr>
<td>Statistical techniques: N/A</td>
</tr>
</tbody>
</table>

**Brown et al, 2007**

Los Angeles
Level 1 trauma center
2003-2004

Inclusion criteria:
• All patients with blunt head trauma and intra-cranial bleed initial CT. Presents data for GCS13-15

Excluded:
• Immediate neurosurgery
• Died within 24 hours
• Does not state just adults but seems only for adults (mean age 44 +/- 19)

Prospective Cohort Study Aim
To identify patients with head injuries that benefit from routine repeat CT imaging

Need for neurological intervention- either medical or surgical (medical= sedatives, mannitol or hyperventilation and surgical= ICP monitor and craniotomy)

Mortality

Age
Gender
Mechanism of Injury
ISS
Admission GCS
Results of CT- interpreted by attending radiologist

Mean/median GCS=14.8
Mean/median age= 56

354 patients all GCS scores with intra-cranial bleed
37 direct to craniotomy
43 dies within 24 hours
274= study population
142/274= mTBI GCS13-15
15/142 had clinical deterioration
27/142 had worse CT scans (only 72/142 had repeat imaging)
5/142 had medical or neurosurgical intervention
3/142 died

Mean/median GCS=14
Mean/median age= 43

**Attrition: Low Risk**

Low risk- inpatient outcomes

Prognostic factor measurement: low risk
Does not really assess prognostic value of factors measured

Outcome measures: Medium risk
No outcome measures after discharge

Confounding Factors: Medium risk
No control for poly-trauma and comorbidities-

Statistical techniques: N/A
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention Details</th>
<th>Number of Patients</th>
<th>Study Recruitment</th>
<th>Attrition</th>
<th>Prognostic factor measurement</th>
<th>Outcome measures</th>
<th>Confounding Factors</th>
<th>Statistical techniques</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas et al 2010</td>
<td>Tennesse Level 1 trauma centre 50 months from Jan 2001</td>
<td>Inclusion criteria: All patients with blunt head trauma and evidence TBI on initial CT. Presents data for GCS13-15 Age 18+ Excluded: Penetrating mechanism Immediate neurosurgery Interventions for unclear indication Died before second CT All patients repeat CT at 6-8 hours after admission</td>
<td>Retrospective Cohort Study To assess whether scheduled repeat CT head imaging is indicated in TBI</td>
<td>Low risk</td>
<td>Low risk</td>
<td>All patients repeat CT at 6-8 hours after admission</td>
<td>Medium risk</td>
<td>N/A</td>
</tr>
<tr>
<td>Klein et al 2010 Israel</td>
<td>3 regional trauma centres in Israel. None had access to neurosurgery on site. Identified ICD9 codes on national trauma registry. Inclusion criteria: GCS13-15 ICD9 code for intra-cranial bleeds. One hospital transferred all patients to neurosurgical centre. Other 2 hospitals transferred selected patients.</td>
<td>Retrospective Cohort Study Aim: Assess the outcome of low risk patients with ICB managed in district hospitals without neurosurgical services</td>
<td>Mortality Neurosurgical intervention Neurological status at discharge</td>
<td>Low risk</td>
<td>Low risk</td>
<td>323 patients all 3 hospital intra-cranial bleed and GCS13-15</td>
<td>Medium risk</td>
<td>N/A</td>
</tr>
<tr>
<td>Study</td>
<td>Level</td>
<td>Trauma Centre</td>
<td>Study Aim</td>
<td>Demographics</td>
<td>Progression of lesion on CT</td>
<td>Surgical intervention- includes intubation</td>
<td>Medical intervention</td>
<td>GOSE at discharge</td>
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<tr>
<td>Sifri et al 2011 USA</td>
<td>Level 1 Trauma Centre New Jersey</td>
<td>2002-2006</td>
<td>Retrospective Cohort Study</td>
<td>Inclusion criteria:</td>
<td>107 patients met inclusion criteria</td>
<td>63/107 worse CT=59%</td>
<td>7/107 neurosurgical group</td>
<td>21/107 deterioration</td>
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<td>Initial GCS 13-15</td>
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<td>Blunt traumatic head injury</td>
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<td>Age 18+</td>
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<td>Intra-cranial injury CT head-ICB or skull fracture</td>
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<td>Repeat CT</td>
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<td>Abnormal neurological examination at time of repeat CT</td>
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<td>Immediate or planned neurosurgical intervention</td>
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<td>Normal neurology at time of repeat CT</td>
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<td>normal neurology defined as GCS15, orientation to place, person or time, normal neurological exam, no symptoms from head injury, headache, vomiting, dizziness, lethargy</td>
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<td>coagulopathy including known bleeding disorder or taking warfarin</td>
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<td>pregnancy</td>
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<td>spinal cord injury</td>
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</table>
Beynon et al 2015 Germany

Inclusion criteria:
- Prior brain surgery
- Acquired or congenital cerebral pathology or existing neurological or psychiatric disorder
- Initial GCS 13-15
- Traumatic Intracranial bleed CT head

Aim: Compare outcomes in patients on different types of anti-coagulants

Repeat CT imaging
Progression on CT Neurosurgery Death
Mean GCS at discharge

Patients divided into those on no anticoagulants, Aspirin, Warfarin and DOACS.
- gender
- trauma mechanism
- comorbidities
- CT findings
- repeated CT imaging, age, GCS scores, laboratory values

70 patients met inclusion criteria
37 no anticoagulation
27 anti-platelets
5 warfarin
6 DOACS (rivaroxaban)
1 patient dabigatran
25% neurosurgery (18 patients)
43/70 repeat CT imaging
2 deaths both on rivaroxaban
Mean/median GCS=14.5
Mean/median age=67
Percent anticoagulated=16

Study Recruitment: Low risk
Although high rates of anti-coagulation.

Attrition: Low Risk
Only inpatient outcome measures

Prognostic factor measurement: Low risk
May be miss-classified in medical notes

Outcome measures: Mod risk
No F/U after discharge

Confounding Factors: Low risk
No control for comorbidities.

Statistical techniques: N/A
None done
## Supplementary Material 2: Data Extracted from Included Studies

### Studies with univariate or multivariate risk factors N=21

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Study Design</th>
<th>Outcome Measures</th>
<th>Prognostic factors assessed</th>
<th>Results</th>
<th>Quality Appraisal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nishijima et al 2014 Sacramento USA</td>
<td>Single-site: Level 1 trauma centre 2009 – 2013</td>
<td>Prospective cohort study</td>
<td>Critical care invention within 48 hours of arrival ED:</td>
<td>Age ≥ 65years</td>
<td>600 patients</td>
<td>Study Recruitment: Mod risk bias Missed 20% eligible patients- not completely clear individuals in cohort identified. Otherwise clear inclusion and exclusion criteria.</td>
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<td>Intubation Neurosurgery including ICP monitoring/ giving mannitol/hy pertonic saline Transfusion RBC/FFP Vasopressor/ ionotrope use Cardiac arrest/ arrhythmia (HR&lt;40, HR&gt;120) Interventional angiography</td>
<td>Sex</td>
<td>71% male</td>
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<td>Dangerous mechanism (any non-fail from standing mechanism)</td>
<td>0.5% died + 6.5% neurosurgery + 8.3% intubated 68% GCS 15</td>
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<td>Pre-injury antiplatelet use (aspirin or clopidogrel)</td>
<td>93% admitted ICU 19.3% had crit care intervention 9.2% transfusion 8.3% intubation 6.5% Neurosurgical</td>
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<td>High risk co-morbidity</td>
<td>4 predictors need for crit care intervention: (Recursive partitioning) GCS&lt;15 (RR 2.95; 95% CI 2.21-4.12) &gt;65years (RR 1.46; 95% CI 1.05-2.03) CT midline shift/absence cisterns (RR 4.11; 95% CI 3.08-5.48) Non-isolated head injury RR (2.74; 95% CI 1.99-3.78)</td>
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<td>ED Vital signs GCS &lt;15 at admission BP&lt;90 at any point ED Sats &lt;95% at any point ED</td>
<td>Sensitivity of decision rule to predict intubation/neurosurgery within 48 hours of admission ED. 98.6% specificity 36.6% To any crit care intervention Sensitivity 98.3% 95% C.I. (93.9-99.5%) Specificity 39.7% 95% C.I. (35.4-44.1%) Positive predictive value 28.1% 95% C.I. (23.9-32.6%) Negative predictive value 99% 95% C.I. (96.3-99.7%)</td>
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<td>Lab results: Platelet count INR Haematocrit</td>
<td>Clinical impression: Do you think patient needs ICU? Sensitivity 90.1% 95% C.I. (83.1-94.4%) Specificity 49.2% 95% C.I. (44.7-53.8%)</td>
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<td>Initial CT: Midline shift/absence cisterns Depressed skull fracture Non-isolated head</td>
<td>Sensitivity 91% 95% C.I. (84.2-95.0%) Specificity 39.5% 95% C.I. (35.1-44.1%)</td>
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<td></td>
<td>Presence of swelling or shift on initial cranial CT RR (95% CI) 4.11 (3.08-5.48) Admission GCS score less than 15 RR (95% CI) 2.95 (2.12-4.12) Non-isolated head injury RR (95% CI) 2.74 (1.99-3.78)</td>
<td></td>
</tr>
</tbody>
</table>

**Aim:** Derive a clinical decision instrument for patients with mild ICH low risk requiring critical care intervention.

**Exclusions:**
- Patients with DNACPR
- Patients pre-injury anti-coagulant use

**Inclusion Criteria:**
- Age ≥ 18 years
- Consecutive patients
- Initial ED GCS 13-15
- CT +ve ICH-axonal injury
- Intra-ventricular, intraparachymal bleed/contusion, diffuse axonal injury

**Statistical Method:**
Derived clinical decision instrument with binary recursive partitioning (misclassification cost 20:1).

**Performance of instrument compared to clinical impression:**
- 6.5% Neurosurgical
- 8.3% intubation
- 9.2% transfusion
- 19.3% had critical care intervention
- 93% admitted ICU
- 92.8% admitted to neo ICU
- 98.6% specificity 36.6%
- 19.3% had critical care intervention
- 9.2% transfusion
- 8.3% intubation
- 6.5% Neurosurgical

### Additional severe injury may be related to prognostic factors and outcome measures. Not accounted for in in analysis.

**Confounding Factors:**
- Mod Risk

**Statistical techniques:**
- low risk

**Overall summary:**
- Risk factors identified by case note review/d/w treating physicians where not clear. Radiology attending written report used for CT findings. No independent quality verification could introduce bias. CT end point also introduce bias. CT end point also introduce bias. CT end point also introduce bias. CT end point also introduce bias.

Mary Ann Liebert, Inc, 140 Huguenot Street, New Rochelle, NY 10801
Sweeney et al 2015

USA

Identified on national trauma database 2007-2012

Inclusion criteria:
- Age ≥ 18 years
- ED initial GCS 14-15
- ICD 9 code intra-cranial injury=
  - SAH, SDH, EDH, multiple TBI
- Admitted to hospital
  - Exclusions:
    - ICD9 diagnoses skull fractures
    - Penetrating mechanism of injury

Retrospective Cohort study

Hypothesis that injury type associated with deterioration in isolated TBI.

Multiple logistic regression used to assess risk of outcomes.

Mixed effects model to explore potential differences between hospitals.

Neurosurgical Intervention:
- Defined as operative procedure, or placement of an ICP monitor. Identified by ICD9 coding.
- Coagulopathy (pooled measure of Vit K deficiency, haemophilia, thrombocytopaenia, chronic anti-coagulant therapy)
- Chronic aspirin use not included.

ISS (measure of head injury severity due to exclusion criteria).

50496 patients met criteria

4474/50496 neurosurg

58% admitted to ICU

EDH-N=901 18% Neurosurg
SDH-N=18784 16% Neurosurg
Mixed N=11984 8% Neurosurg
SAH N=13191 1.5% Neurosurg
Contusion N=5636

Data set split into 2/3 training set and 1/3 test set.

Adjusted odds ratios for neurosurgical procedures. Multiple logistic regression run on 2/3 training set (n = 33,327)

Age (years) OR=1.002 (95% CI0.999 – 1.01) P=0.18
Anticoagulation Disorder OR=0.853 (95% CI 0.66 – 1.09) P=0.21
ED GCS OR=0.894 (95% CI 0.781 – 1.03) P=0.11
ED Systolic Blood Pressure OR=1.004 (95% CI 1.002 – 1.01) P<0.001
ED Pulse OR=0.99 (95% CI0.986 – 0.993) P<0.0001
ED Respiratory Rate OR=0.962 (95% CI0.944 – 0.98) P<0.0001

Study Recruitment: High risk bias

Eligible patients recruited through a relatively new national trauma database by ICD9 coding. Potential selection bias as to which hospitals upload data. Also uncertain how accurate coding is.

Excluded patients with incomplete data, they may be systematically different.

Attrition: Low risk

As a trauma registry represents routine information that should be consistently on all eligible patients.

Prognostic factor measurement: Mod risk

Grouping of coagulopathy problematic, different likely risk of warfarin versus ITP for example. CT findings watered down to code for injury, misses important findings.

Outcomes out 48 hours too short, also crit care intervention definition very broad- e.g. transfusion. No blinding to exposure/outcomes.

Overall good internal validity of study. But issues with generalising results:
- Exclusion of anti-coagulated patients.
- Short outcome measurement 48 hours.
- Outcome measures of critical care intervention quite soft- including transfusion of blood products.
- No external validation of results.

JET W 2013

TBI 31,634

Inclusion criteria:
- Age > 18 years
- ED initial GCS 14-15
- ICD 9 code intra-cranial injury=
  - SAH, SDH, EDH, multiple TBI
- Admitted to hospital
  - Exclusions:
    - ICD9 diagnoses skull fractures
    - Penetrating mechanism of injury

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Hypothesis that injury type associated with deterioration in isolated TBI.

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Mixed effects model to explore potential differences between hospitals.

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- Short outcome measurement 48 hours.
- Outcome measures of critical care intervention quite soft- including transfusion of blood products.
- No external validation of results.
AIS score >1 any other body region

Data missing ED vital signs

ISS 7-11 OR=2.35 (95% CI 1.44 – 4.09) P<0.01
ISS 12-18 OR=3.37 (95% CI 2.06 – 5.86) P=0.0001
ISS 19-27 OR=18.9 (95% CI 11.6 – 33) P<0.0001
ISS >27 OR=7.01 (95% CI 3.79 – 13.4) P<0.0001

Injury Category (vs. Contusion)

Isolated SAH OR=0.95 (95% CI 0.64 – 1.41) p=0.79
Isolated SDH OR=4.9 (95% CI 3.61 – 6.84) P<0.0001
Isolated EDH OR=6.42 (95% CI 4.15 – 9.97) P<0.0001

Multiple Injury Types OR=2.34 (95% CI 1.7 – 3.29) P<0.0001

After adjustment injury severity, age, coagulopathy and ED vital signs: injury pattern significantly associated need for neurosurgery: OR EDH versus contusion 6.4 (95% CI 4.1-9.9).

Age no association.

ED vital signs also predictive.

In test AUC ROC curve = 0.81 in test set
Hosmer-Lemeshow P = 0.8 in test set

38% expected and observed rate of neurosurgery highest risk decile. O.5 % in lowest risk decile.

Mean/median age = 61
Percent anticoagulated=5

Outcome measures: Moderate risk
Need for neurosurgery only as recorded on trauma data bank, possibly unreliable. Misses other important adverse outcome e.g. death and intubation. Does not include time scale from presentation or what happens to patients who are discharged and re-attend with adverse outcome. Follow up not clear

Confounding Factors: Low risk
Excluded other injuries and made adjustments in logistic regression model. No attempt to control for co-morbidities.

Statistical techniques: low risk
Good presentation of methods
Finds that injury type significantly associated with need for neurosurgery -provides candidate factors. There are methodological problems with paper.

Joseph et al
2015
USA
Retrospective case note review 2009-2012
Inclusion criteria:
- Initial GCS13-15
- Aged 18+
- Initial scan +VE ICH/skull fracture and routine repeat

Method
All patients underwent routine repeat CT

Progression on repeat CT
Neurosurgical intervention= craniotomy or craniectomy as inpatient

Age
Gender
Race
Ethnicity
Mechanism of injury
GCS
BP
HR
FBC
Serum lactate
Base deficit
AIS
ISS
CT findings reviewed by an investigator that

876 patients met inclusion criteria

115 (13.1%)=progression on CT

Univariate predictors:
Age 65+ p=0.07 OR1.5(0.9-2.5)
Male p=0.8 OR1.1 (0.6-1.7)
Intoxication p=0.9 OR1.3 (0.3-4.7)
Mechanism of injury p=0.5 OR 1.1 (0.3-2.8)
HR>100 p=0.7 OR1.1 (0.6-1.8)
BP<90 p=0.35 OR 1.3 (0.45-1.9)
LOC p=0.2 OR1.2 (0.6-2)

Displaced skull fracture P=0.02 OR 1.9 (1.1-3.3)
SDH >10mm p=0.004 OR3.4 (1.5-8)
EDH >10mm p=0.01 OR3.8 (1.2-7.6)
Hgb<10 P=0.4 OR 1.5 (0.76-3.1)

Study Recruitment: Mod risk
Retrospective identification of case notes- depends on accuracy of case notes

Excludes patients on anti-coagulants and anti-platelets

Attrition: low risk
Outcomes only as inpatients

Prognostic factor measurement: Low risk
Relies on accuracy of medical notes.

Re-examines CT images

Information.
| Imaging within 6 hours of initial CT imaging. | Imaging still showed injury.  
- Isolated TBI as defined head AIS greater/equal 3 and AIS <3 other body regions. 
- Excluded:  
  - On Anti-platelets  
  - On Anti-coagulants  
  - Transfers  
  - Needed immediate neurosurgery. |
|---|
| was part of the team-classified size of lesion and whether progression on CT | Platelets less than 100000 p=0.04 OR 1.5 (1.1-3.9)  
Lactate <=2.5 p=0.18 OR 2.6 (1.2-5.5) (?!)
Base deficit>4 p=0.02 OR 3.1 (1.2-7.6)

**Multi-variate Analysis:**
Age 65+  P=1.4 OR 1.4 (0.7-2.7)  
LOC P=0.8 OR 1.1 (0.5-2)  
Displaced skull fracture P=0.08 OR 2.3 (0.9-3.5)  
SDH>10mm P=0.007 OR 4.8 (1.9-9.6)  
EDH>10mm P=0.001 OR 7.9 (2.4-12.6)  
Platelets less than 100000 p=0.1 OR 1.3 (0.9-3.6)  
Lactate <=2.5 p=0.2 OR 2.1 (0.89-2.5)  
Base deficit>4 p=0.01 OR 2.8 (1.6-4.1)

**47 (5.4%) = neurosurgery**

**Univariate predictors:**
Age 65+  p=0.3 OR 1.08 (0.8-1.3)  
Male  p=0.19 OR 1.2 (0.8-1.3)  
Intoxication  p=0.3 OR 1.8 (0.9-3.4)  
BP<90  p=0.35 OR 1.3 (0.45-1.9)  
Mechanism  p=0.34 OR 1.2 (0.4-1.8)  
LOC  p=0.39 OR 1.4 (0.7-3.2)  
HR>100  p=0.26 OR 1.5 (0.9-2.8)  
Displaced skull fracture  p=0.01 OR 16 (7.6-19.6)  
SDH>10mm  p=0.001 OR 3.9 (2.4-5.1)  
EDH>10mm  p=0.03 OR 4.8 (2.9-5.6)  
Hgb<10  p=0.51 OR 1.2 (0.6-2.5)  
Platelets less than 100000 p=0.31 OR 2.5 (1.15-5.1)  
Lactate <=2.5 p=0.12 OR 3.6 (0.7-6.5)  
Base deficit>4 p=0.01 OR 23 (1.6-31)

**Multi-variate Analysis:**
Male  p=0.1 OR 1.6 (0.8-2.1)  
LOC  p=0.3 OR 1.2 (0.5-1.9)  
Displaced skull fracture  p=0.001 OR 10 (6.7-12)  
SDH>10mm  p=0.001 OR 3.4 2.1-4.46)  
EDH>10mm  p=0.006 OR 3.5 (1.4-5.5)  
Platelets less than 100000 p=0.09 OR 1.3 (0.98-4.8)  
Lactate <=2.5 p=0.21 OR 1.9 (0.62-3.1)  
Base deficit>4 p=0.001 OR 21 (1.6-27)

**Mean/median GCS=14.3**

**Outcome measures:**
Mod risk  
Only measures as inpatient. Potential for discharge and deterioration.

**Confounding Factors:**
Low risk  
Possibility of confounding due to other comorbidities- does not adjust for this,

**Statistical techniques:**
Mod risk  
Some of the results appear to be reported wrong. E.g. Lactate

**Overall:**
Presents useable data for analysis

Note base deficit found to be highly prognostic- only study to assess this.
<table>
<thead>
<tr>
<th>Borczuk et al 2013</th>
<th>Level 1 trauma centre Boston USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case note review 2009-2010 patients identified through ED electronic coding ICD9 coding for intra-cranial haemorrhage.</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td><strong>Described as a cross sectional study</strong></td>
</tr>
<tr>
<td>• GCS 13-15</td>
<td>Seems more like a retrospective cohort study Aims Develop a set of criteria to identify patients who are at low risk for deterioration and thus may not require neurosurgical evaluation</td>
</tr>
<tr>
<td>• Age 15 or older</td>
<td>Method Univariate analysis to predict composite outcome of deterioration</td>
</tr>
<tr>
<td>• CT positive traumatic intra-cranial haemorrhage</td>
<td>CT categorised by attending radiologist type, location and size of bleed/contusion. Presence of midline shift</td>
</tr>
<tr>
<td>Excluded:</td>
<td>3 factor multivariate model derived from univariate analysis</td>
</tr>
<tr>
<td>• Isolated Skull fractures</td>
<td>Deterioration whilst in hospital including: Decrease in GCS Worsening neurological examination Worsening CT result on repeat CT Neurosurgery Death</td>
</tr>
<tr>
<td></td>
<td>Composite outcome All outcomes whilst in hospital no discharge outcomes</td>
</tr>
<tr>
<td></td>
<td>Data extracted from case notes by 2 ED researchers. Not blinded to the hypothesis</td>
</tr>
<tr>
<td></td>
<td>Age</td>
</tr>
<tr>
<td></td>
<td>Method of arrival</td>
</tr>
<tr>
<td></td>
<td>History of HTN</td>
</tr>
<tr>
<td></td>
<td>Anti-coagulation</td>
</tr>
<tr>
<td></td>
<td>Mechanism</td>
</tr>
<tr>
<td></td>
<td>Initial GCS</td>
</tr>
<tr>
<td></td>
<td>Neurological examination</td>
</tr>
<tr>
<td></td>
<td>Alcohol Intoxication</td>
</tr>
<tr>
<td></td>
<td>Initial platelet count</td>
</tr>
<tr>
<td></td>
<td>INR</td>
</tr>
<tr>
<td></td>
<td>Initial CT result</td>
</tr>
<tr>
<td></td>
<td>F/U CT result</td>
</tr>
<tr>
<td></td>
<td>404/863 TBI patients met inclusion criteria (46.8% patients with traumatic bleeds).</td>
</tr>
<tr>
<td></td>
<td>11.8%(48) deteriorated</td>
</tr>
<tr>
<td></td>
<td>5.9% neurosurgical</td>
</tr>
<tr>
<td></td>
<td>Deterioration stratified by injury: 24/136 isolated SDH 0/1 isolated EDH 1/75 isolated SAH 2/31 contusions 22/161 mixed lesions</td>
</tr>
<tr>
<td></td>
<td>Univariate predictors of deterioration:</td>
</tr>
<tr>
<td></td>
<td>Age 65+ OR 0.93 95% CI 0.5-1.69</td>
</tr>
<tr>
<td></td>
<td>Sex OR 0.77 95% CI 0.41-1.41</td>
</tr>
<tr>
<td></td>
<td>Fall OR 0.57 95% CI 0.29-1.09</td>
</tr>
<tr>
<td></td>
<td>Assault OR 1.07 95% CI 0.45-2.51</td>
</tr>
<tr>
<td></td>
<td>RTC OR 0.51 95% CI 0.12-2.21</td>
</tr>
<tr>
<td></td>
<td>Pedestrian Struck OR 1.12 95% CI 0.32-3.92</td>
</tr>
<tr>
<td></td>
<td>Bicycle Struck OR 1.51 95% CI 0.42-5.44</td>
</tr>
<tr>
<td></td>
<td>HTN OR 0.94 95% CI 0.51-1.73</td>
</tr>
<tr>
<td></td>
<td>Aspirin OR 0.79 95% CI 0.41-1.51</td>
</tr>
<tr>
<td></td>
<td>Warfarin OR 0.87 95% CI 0.33-2.32</td>
</tr>
<tr>
<td></td>
<td>Clopidogrel OR 1.25 95% CI 0.27-5.75</td>
</tr>
<tr>
<td></td>
<td>GCS&lt;15 OR 2.12 95% CI 1.01-4.43</td>
</tr>
<tr>
<td></td>
<td>CT findings</td>
</tr>
<tr>
<td></td>
<td>Any lesions</td>
</tr>
<tr>
<td></td>
<td>SDH OR 2.64 95% CI 1.20-5.83</td>
</tr>
<tr>
<td></td>
<td>EDH OR 2.4 95% CI 0.91-6.31</td>
</tr>
<tr>
<td></td>
<td>SAH OR 0.42 95% CI 0.22-0.81</td>
</tr>
<tr>
<td></td>
<td>Contusion OR 0.79 95% CI 0.39-1.62</td>
</tr>
<tr>
<td></td>
<td>Isolated lesions</td>
</tr>
<tr>
<td></td>
<td>SDH OR 1.62 95% CI 0.88-2.96</td>
</tr>
<tr>
<td></td>
<td>EDH OR only 1 patient</td>
</tr>
<tr>
<td></td>
<td>SAH OR 0.078 95% CI 0.01-0.59</td>
</tr>
<tr>
<td></td>
<td>Contusion OR 0.46 95% CI 0.11-1.96</td>
</tr>
<tr>
<td></td>
<td>Multiple logistic regression with 3 variables GCS=15, presence SDH and presence isolated SAH:</td>
</tr>
<tr>
<td></td>
<td>All remained significant predictors of deterioration. Sensitivity 97.9% and specificity 20.8%</td>
</tr>
</tbody>
</table>

**Mean/median age= 54**

**Percent anticoagulated=0**

**Study Recruitment: low risk**

Dependent on how good electronic coding is and case note review was.

**Attrition: Low risk**

Follow up only for period in hospital

**Prognostic factor measurement:**

**Low risk**

Written CT reports from attending radiologist used for data extraction. No verification of accuracy or consistency.

**Outcome measures:**

**Mod risk**

No F/U following discharge- missed delayed outcomes, could have looked for re-attendance. GCS and neurological examination also potentially subjective.

**Confounding Factors:**

**Mod risk**

No attempt to control or exclude polytrauma patients or patients with multiple comorbidities

**Statistical techniques:**

**Mod risk**

Good univariate analysis Small number prevented large enough multi-variate model
Aim: To determine if there exists a sub-population of mild TBI patients with an abnormal head CT scan that requires neither repeat brain imaging nor admission to an ICU.

Standard of care is to admit these patients to ICU and routinely re-CT.

Methods: Univariate and multivariate analysis for outcomes of interest.

Neurological or medical decline.

- The need for neurosurgical intervention.
- The GOS score.
- Neurological decline was defined remaining in the ICU or transfer back to an ICU or intervention as a result of a decline in mental status or the development of a neurological deficit.
- Medical decline was defined as increase in monitoring or intervention due to cardiac, pulmonary, or renal decline.

Outcome measures during admission and at discharge.

Age, Sex, Injury mechanism Initial GCS score Duration of hospital stay. Aspirin/Clopidogrel/ Warfarin use Ttransfusion of blood products Intubation CT scans classified into Marshall and Rotterdam Criteria-blinded assessment by author

321 patients met the inclusion criteria

Neurological decline 1% 4
Surgical intervention 1%
Medical decline 6% 18
Cardiac event 7%
Respiratory event 4%
Seizure event 2%
CT progression 6%

GOS score at discharge:
1 1%
2 0%
3 4%
4 10%
5 85%

Age + transfusion predictors of a medical decline (p < 0.01).

Odds ratio of having a medical decline after undergoing a blood product transfusion was 12.55 (95% CI 4.3–36.7).

Cardiac and respiratory events the odds ratios were 5.6 (95% CI 2.4–13.1) and 8.8 (95% CI 2.6–30.4).

Significantly higher mortality transfused group as compared with the non-transfused group (6% vs 0%, respectively, p < 0.0001, Fisher exact test).

Higher rate of brain injury progression in the transfused patients (13% vs 5%, p = 0.04).

Predictors of bleed progression univariate analysis:
ICH vol >10 ml OR 20.13 95% CI (5.67–71.44)
subfrontal/temporal contusion OR 5.73 95% CI (2.20–14.89)
age ≥65 yrs OR 4.00 C.I (1.40–11.42)
antiplatelet &/or Coumadin therapy OR 2.94 C.I (1.12–7.71)

Negative predictive value 99.6% Positive predictive value 38.8%
Mean/median GCS=14.8 Mean/median age =60
Percent anticoagulated=10

Study Recruitment: low risk
Through case note review-potential for patients without notes to be missed

Attrition: low risk
Follow up only for period in hospital

Prognostic factor measurement: Low risk
Case note extraction- potentially incomplete
CT scans re-reported. Uses Marshall classification

Outcome measures: Mod risk
Outcome measures only during hospital admission. No measure of re-attendance or community outcome F/U.
The outcome measures of neurological and medical decline are subjective.

Confounding Factors: Medium risk
No control for other injuries and comorbidities

Statistical techniques: High risk
Selective reporting of significant risk factors and does not present full analysis. No analysis to predict neurosurgical outcomes.

Potentially can re-analyse the data from what is presented
independently associated with the risk of hemorrhagic progression. Patients with a hemorrhage volume > 10 ml were 20.13 times more likely to have progression on head CT.
Mean/median GCS=14.8
Mean/median age=57

Choudhry et al 2013
USA
Identified Search Strategy
Level 1 trauma center
New Jersey
Retrospective cohort patients in trauma data base 2002-2006
Inclusion criteria:
• GCS>12
• Initial scan +VE ICH
Excluded:
• Discharged
• Pregnancy
• Needed immediate neurosurgery
• Spinal cord injury
• Brain surgery or existing cerebral pathology
• Chronic neurological/psychiatric disorder e.g. dementia
• Incomplete medical records
• Use of sedating drugs
Age range 18-90 in results

Retrospective cohort study using trauma data base.

Objective: To identify the cause, temporal course and outcomes of patients who deteriorate neurologically after presenting with MHI and ICH

Methods:
Presents univariate and multivariate risk of death

Outcome measures:
Delayed neurological deterioration defined as: GCS drop 2 or more points for more than 1 hours New focal neurological deficit

Collected data: Age, Sex, Ethnicity, Mechanism of injury, GCS, AIS, Coagulopathy

908 patients MHI and ICH
151 not included due to incomplete notes or meeting exclusion criteria
757= final cohort
31/757= delayed deterioration at inpatient. 4.1% (21 due to progression ICH, 10 due to medical causes)
7/757 deaths
21/757 patients worse CT scans

Univariate analysis outcome death
Age/>=60 P=0.001
Coagulopathy P=0.02
Increase Marshall classification repeat CT P=0.001
Decline in consecutive GCS scores more than 6 P=0.02
Deterioration within 9 hours P=0.04
H-AIS>3 P=0.32
ISS>20 P=0.38
Initial GCS<i>15 P=0.40
Initial Marshall classification >II P=0.41
Age>60 predicted deterioration due to expansion of bleed and death in stepwise logistic regression (p<0.01)
Mean/median age=49

Study Recruitment: Mod risk
Retrospective identification of patients on trauma database. Relies on patients being correctly recorded on this. Patients with incomplete notes excluded- may be systematically different.

Attrition: low risk
Reports no loss to F/U at 6 months routine clinic- may form part of group of patients excluded due to incomplete notes

Prognostic factor measurement: Low risk
Relies on accuracy of medical notes

Outcome measures: Mod risk
Outcome measure of delayed deterioration- relies on adequate checks on patients and neurological examinations in a consistent way. Assumes this is baseline level of care- likely to vary dependent on where the patients were admitted (e.g. ICU versus normal hospital bed)

Confounding Factors: low risk
Doesn't explicitly say for patients with only a head injury, if does include other injuries high risk for confounding.
Also no adjust for comorbidities

Statistical techniques: High risk
Univariate outcomes for mortality
| Kim et al 2014 South Korea | University hospital Seoul South Korea Case note review from Jan 2002-Dec 2012 Inclusion criteria:  All patients with acute traumatic subdural bleeds Excluded:  Neurosurgery within 24 hours of admission  GCS<13 on admission  Patients with vascular abnormalities  Subdural localised to the falx/tentorium cerebelli  Bilateral subdurals  Aged less than 98 patients included | Delayed surgical evacuation of subdural haematoma | Age Gender Cause of trauma Presence of other CT findings Neurological deficit Comorbidities History of antplatelets Anticoagulation therapy INR Platelet count | 51/98 progression on CT either at 1 week, 2 weeks or 3-10 weeks. 34/98 delayed surgical evacuation up to 10 weeks following trauma Univariate comparison between conservative and delayed neurosurgical group: Mean age P=0.375 Male, P=0.950 Glasgow Coma Scale P=0.647 Hypertension P=0.883 Diabetes P=0.785 Smoking P=0.107 Alcohol abuse P=0.840 Use of anticoagulant P=1.000 Use of antplatelet agent P=0.546 Thrombocytopenia (<50,000) P=1.000 Prolonged prothrombin time (INR>1.4) P=0.656 Cause of head trauma P0.651: Fall from standing Motor vehicle accident Fall from a height Assault Bicycle accident Mean SDH maximal thickness (mm, range) P<0.001* Mean SDH volume (ml, range) <0.001* Mean midline shift (mm) P=0.001* Presence of cerebral contusion P=0.003* | Study Recruitment: Low risk Retrospective case note review—depends on information being recorded correctly. Attrition: low risk All patients appeared to have been followed up appropriately Prognostic factor measurement: Low risk Appears CTs have been reviewed and volume measurements conducted by member of study team Outcome measures: Low risk All patients followed up until clinic. No reports of deaths. Confounding Factors: Low risk None obvious—exclude patients with other injuries Statistical techniques: Low risk Well presented Overall Only patients with subdural—have been shown to high risk in other performed multivariate stepwise regression—only one result without confidence intervals.

Overall

Compares patients with medical and neurosurgical deterioration and that died and didn’t die with worsening CT scans. Much more pertinent to compare patients that deteriorated and didn’t deteriorate.
### Multivariate analysis of prediction of delayed haematoma evacuation.

<table>
<thead>
<tr>
<th>Outcome measured</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal thickness</td>
<td>0.527 (0.5-41.1)</td>
</tr>
<tr>
<td>Volume haematoma</td>
<td>0.01 (1.02 -1.17)</td>
</tr>
<tr>
<td>Midline shift</td>
<td>0.01 OR=1.43 (1.09-1.89)</td>
</tr>
<tr>
<td>Cerebral contusion</td>
<td>0.92 OR 0.85 (0.18-3.97)</td>
</tr>
<tr>
<td>SAH</td>
<td>0.43 OR 0.53 (0.11-2.56)</td>
</tr>
</tbody>
</table>

### Presence of SAH, Presence of Diffuse cortical atrophy, Mean bifrontal ratio (range)P= 0.345 Mean Sylvian fissure ratio (range) P=0.602

### Other significant injuries

- Patients refusing surgery

### Multivariate regression analysis to predict GOS >3 (full recovery)

- Admission Trauma surgeon P=0.3 OR 1.74 (0.61–4.92)
- Age P<0.001 OR0.94 (0.91–0.96)
- ISS P=0.001 OR0.87 (0.81–0.94)
- GCS P=0.005 OR13.96(2.3–87.3)

### Outcome measures: mod risk

- Mean/median GCS=14.7
- Mean/median age= 49

### Study Recruitment: Mod risk

- Retrospective case note review-depends on information being recorded correctly.
- Only patients with bleed less than 1cm

### Attrition: Mod risk

- Not clear when outcomes measured- if at discharge low risk

### Prognostic factor measurement: Low risk

- Doesn’t explain how CT reports interpreted and how 1cm cut off decided.

### Outcome measures: mod risk

- States GOS- but not when or who determined score ?self reported

### Confounding Factors: Mod risk

- None obvious

### Statistical techniques: Mow risk

- States backward step binary logistic regression analysis performed to assess trauma surgeon versus neurosurgical admissions- controlled for age, sex,
| Schwed et al 2016 | UCLA California USA | Level 1 trauma centre 2012-2015 | **Inclusion criteria:**
- Patients identified on trauma registry and case note review
- Initial GCS 13-15
- Intra-cranial bleed: any variety identified by CT imaging
- Excluded:
  - Transfers
  - Not admitted to ICU
  - Required emergent neurosurgery
  - Patients less than 18
  - In police custody
  - Pregnant

| **Aim** | Identify admission variables associated with favourable outcomes with mTBI and intracranial haemorrhage |
| **Method** | Univariate and multi-variate regression analysis prediction of “favourable outcome composite measure” |

| **Vital signs** | AIS, ISS, CT findings-Marshall and Rotterdam scores |

| **Favorable outcome composite measure of following:**
- Alive at discharge
- ICU admission for less than 24 hours
- No in hospital complications
- Did not require neurosurgery
- Failed to achieve this if required ventilation or ionotropic support at any point.

| **380 TBI patients in study period** |
| **19 missing records** |
| **201 remaining cohort met inclusion/exclusion criteria** |
| **4/201 deaths (2 attributable to bleed progression)** |
| **129/201 GCS 15** |
| **6/201 neurosurgical outcomes** |
| **21% (42) in hospital complication** |
| **78/201 met conditions favourable outcome** |
| **0/1 EDH favourable outcome** |
| **1/4 ICH favourable outcome** |
| **18/36 SDH favourable outcome** |
| **30/57 SAH favourable outcome** |
| **21% (42) in hospital complication** |
| **22/83 mixed lesions favourable outcome** |
| **123/201 unfavourable outcome** |

Univariate comparison between patients with favourable and unfavourable outcomes:
- Age P=0.01
- ISS P=0.001
- Head AIS P=0.026
- Time to first head CT (hours) non-significant
- ED systolic blood pressure P=0.01
- ED heart rate P>0.48
- Marshall score P=0.11
- GCS at time of admission ICU P <0.0001
- GCS 15 at admission P=0.0001
- Type of hemorrhage
  - Epidural P=0.42
  - IVH P=0.55
  - SDH P=0.1

Study Recruitment: Mod risk
- Only admitted to ICU- higher risk group than total population.

Attrition: Low Risk
- Only inpatient measures

Prognostic factor measurement: Mod risk
- Does not assess pupillary response or anticoagulation/antiplatelets

Outcome measures: Mod risk
- Only inpatient related outcome measures.

Confounding Factors: Mod risk
- Cohort includes patients with multiple injuries- 2 deaths appear due to factors unrelated to head injury

Statistical techniques: Mod Risk
- Selective reporting of significant results.

- Does present statistical comparison between the groups with favourable and unfavourable outcomes
### Thorson et al. 2012
Miami Level 1 trauma centre 1996-2010

#### Inclusion criteria:
- Initial GCS 13-15
- Present on trauma registry
- Head abbreviated AIS 1 or greater
- No other injuries (AIS = 0 other body regions)
- Repeat CT head scan if intracranial injury detected (4-6 hours after initial CT)

#### Methods
- Step wise multivariate regression for factors P < 0.2 associated with progression on CT and craniotomy
- Neurosurgical intervention.
- Death.

#### CT findings:
- Including type of injury, presence of oedema, mass effect or herniation.

#### Progression of initial lesion or new lesion identified.

### Retrospective cohort study

#### Aim
- To test whether routine CT imaging in mTBI with detected intracranial injuries provides useful information in the absence of neurological deterioration

### Study Recruitment: High risk
Neurosurgeon have selected out patients with “trivial” injuries — makes this a higher risk group than population of interest

### Attrition: Low Risk
Only inpatient measures

### Prognostic factor measurement: Low risk
Loose definition for abnormal neurology

### Outcome measures: Mod risk
Only inpatient related outcome measures.

### Confounding Factors: Low risk
None obvious

### Statistical techniques: Mod Risk
Selective reporting of outcomes in regression model

### Paper concludes all patients should have a repeat CT as 7/360 patients had neurosurgery based solely on repeat CT head findings.

### Possibly include but is a higher risk
lesion was to insignificant to warrant a repeat CT
Excluded:
- Penetrating trauma
- Pregnant
- Age<18
- Incarcerated
- Transfers

30/360 neurosurgical outcomes
Age
No Neuro Surg
21
51
D
23
P=0.97
Sex
No Neuro Surg
Male
241
Neuro Surg
22
P=0.11
ISS
No Neuro Surg
13
5
SD
5
13
P=0.01
GCS 15
arrival Neuro Surg
180
Neuro Surg
13
GCS 14
No Neuro Surg
100
Neuro Surg
8
GCS 13
No Neuro Surg
50
Neuro Surg
9
Anticoagulant Use
No Neuro Surg
22
Neuro Surg
6
0.024
Aspirin
No Neuro Surg
9
Neuro Surg
n
3
Plavix
No Neuro Surg
2
Neuro Surg
2
Coumadin
No Neuro Surg
2
Neuro Surg
4
LMWH
No Neuro Surg
2
Neuro Surg
0
Multiple No Neuro Surg
4
Neuro Surg
2
PT No Change
12.1
Progression
12.0
P=0.35
PTT No Change
25
Progression
27.5
P=0.45

7/30 operated patients solely on basis of worse CT (no prior neurological decline)
22/360 deaths

Logistic regression analysis: unclear which factors were tested in the model
Predictors of worse 2nd CT AU ROC curve 0.703
GCS=13 OR 4
95% CI 2.02-7.93
P=0.001
GCS=14 OR 3.11
95% CI 1.77-5.48
P<0.001
ISS OR 1.07
95% CI 1.02-1.11
P<0.001
Mass effect OR 2.02
2.02-3.78
P<0.001

Predictors of craniotomy: AUC ROC 0.849
Initial mass effect OR 5.24
95% CI (1.96-14.1)
P=0.001
New/worse EDH 2nd CT OR 23.3
3.67-148.3
P=0.001
New/worse mass effect 2nd CT 5.73
1.64-20)
New/worse herniation 32.1
7.83-131.6
P=0.001

Study Recruitment: Low risk
Identified from prospective trauma registry: dependent on how accurate this is
Attrition: Mod Risk
Not clear whether and when all patients followed up but presents outcomes from outpatient clinic
Prognostic factor measurement: population given selection out of patients with “non-significant” findings.
Note also 11% of 360 repeat CTs recalled-i.e. initial finding not present (4/6 hours after injury).

Quigley et al 2012 Pennsylvania Level 1 trauma centre 2004-2011
All patients admitted ICU for at least overnight observation
Inclusion criteria:
- Retrospective Cohort Study
- Aim To assess if traumatic subarachnoid haemorrhage more benign form of mTBI
- Multivariable
- Discharge home Clinical deterioration CT progression Neurosurgery
- Demographics Mechanism of injury Number and results of follow up CT Length of hospital and ICU admission ISS
- CTs re-reviewed by study radiologist
- 547 patients identified as subarachnoid
- 478/547 isolated subarachnoid
- 470/478 repeat CT imaging
- 15/470 worse CT (1 is new stroke)
- 342/478 discharged home
- 51/478 discharged rehab or nursing home
- 4/478 self discharge
- 4/479 long term care facility
- 1/479 other facility
- 5/479 patients died
<table>
<thead>
<tr>
<th>Study Title</th>
<th>Institution</th>
<th>Methodology</th>
<th>Inclusion Criteria</th>
<th>Analysis</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velmahos et al 2006</td>
<td>Massachusetts Level 1 trauma centre 2003-2004</td>
<td>Retrospective cohort study</td>
<td>All patients with intra-cranial injuries identified reviewed by a neurosurgeon and repeat CT scheduled within 24 hours.</td>
<td>Present on trauma registry, Initial GCS13-15, Isolated subarachnoid haemorrhage, Does not state adult only but mean age 65.7</td>
<td>Discharge to hospice 1/479, 6 week follow up 1/478 bilateral subdural- drained States surgical intervention 0.2% Step down Multivariate regression with outcome discharge home Age P&lt;0.0001 Admission GCS P=0.0018 ISS P=0.0088 Not progression of bleed on CT</td>
</tr>
</tbody>
</table>

**Low risk**
- Ct scans reviewed
- Outcome measures: Mod risk
- Not clear if uniform outpatient followup
- Confounding Factors: High risk
- Clearly an old patient population discharge to rehab/nursing home like related comorbidities or other injuries
- Statistical techniques: High Risk
- Selective reporting of outcomes in regression model
- No confidence intervals or odds ratios.
- No explanation of high the model was derived

**General comments:**
- Discharge outcomes contradict low level of intervention.
- Unable to pool risk factors as are. Can pool to confirm Subarachnoids are low risk.

**Study Recruitment:** Low risk
- Identified from trauma registry-dependent on how accurate this is
- Standard model of care for all patients

**Attrition:** Low Risk
- Appears only inpatient outcomes

**Prognostic factor measurement:**
- Mod risk
- Assessment of time to CT - not clear biological mechanism how this affects outcome or how measured

**Outcome measures:** Mod risk
- Takes reports from attending at face value.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Inclusion criteria</th>
<th>Aim</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabbri et al 2013</td>
<td>Multi-centre multicentre cohort study</td>
<td>Any GCS &gt;18, head abbreviated AIS ≥1 or greater, no indication for neurosurgery within 7 days</td>
<td>To assess whether pre-injury antiplatelet use lead to worse outcome in patients with intra-cranial injuries detected by CT imaging</td>
<td>Worse repeat CT defined as increase point on Marshall criteria within 24 hours, neurosurgery within 7 days, GOS at 6 months</td>
</tr>
</tbody>
</table>

**Retrospective multicentre cohort study**

**Aim**
- To assess whether pre-injury antiplatelet use lead to worse outcome in patients with intra-cranial injuries detected by CT imaging

**Outcome measures**
- Age
- Sex
- Mechanism
- Coagulation
- GCS
- Anti-platelet medications
- Type of injury on CT
- Marshall Classification

**Study of all GCS patients but present data for GCS 14-15:**
- 1123/1558 patients GCS 14-15
- Antiplatelet therapy increased the risk of a worse CT:
  - RR 1.86 95% CI 1.06-3.30 P=0.032
  - RR 3.34 95% CI 1.74-6.40 P=0.003

**Mean/median age= 65**

**Prognostic factor measurement:**

**Does not report deaths as a primary outcome but included in table- not clear what the cause of deaths is.**

**Confounding Factors: High risk**
- Not isolated head trauma and no selection out of comorbid patients- does not appear deaths related to head injury but clear

**Statistical techniques: Mod Risk**
- Selective reporting of outcomes in regression model

**General comments:**
- Time to initial CT highly significant- slightly odd for this study population- not examined any other study.
- No explanation for deaths given in paper.
### Inclusion criteria:
- Acute TBI and intracranial haemorrhage (epidural, subdural, intra-cerebral or SAH)
- Adult age range 15-75 in study

### Excluded:
- Penetrating injury
- GCS <13
- Immediate neurosurgery
- Chronic bleed

### Aim
Determine the potential risk factors of delayed neurosurgical intervention in mTBI with intracranial haemorrhage

### Stepwise logistic regression to identify variables that predicted failure of conservative treatment

### Neurologic deterioration-GCS drop 2+ points, seizures, signs raised ICP
Repeat CT if deterioration—whether worse

### Neurosurgical intervention— including craniotomy, craniectomy

### Sex
- Age
- Mechanism of injury
- GCS
- ISS
- Laboratory results including clotting CT results as reviewed by investigator

### Outcome measures:
- 340 patients met inclusion criteria
- 13/340 neurosurgical outcomes
- 25/340 neurological decline
- 7/118 mixed lesions neurosurgery
- 34/340 worse CT
- 3/340 died

### Univariate analysis: delayed neurosurgery versus non-neurosurgery
- Median age P=0.082
- Male/female P=0.573 OR 0.648 95% CI 0.196–2.149
- GCS P= 0.189
- Anti-platelet and/or warfarin therapy P=0.403 OR 2.188 95% CI 0.263–18.222
- Statin therapy P= 1.000
- Hypotension 0 4 P= 1.000
- WBC count (1000/mL) P= 0.023
- RBC count (1000/mL) p=0.401
- Hemoglobin, P=0.606
- Coagulopathy P=1.000
- Hypertension P=0.526 OR 0.484 95% CI 0.196–2.149
- Diabetes mellitus P=1.000 OR 1.028 95% CI 0.221–4.780 (??)
- Old cerebral vascular accident=1.000
- Coronary artery diseases P=1.000
- Arrhythmia P=1.000
- Liver cirrhosis P=1.000

### Study Recruitment: Lod Risk
No uniform criteria for which patients undergo immediate neurosurgery- just selected by neurosurgeon

### Attrition: Low Risk
Only inpatient measure

### Prognostic factor measurement: Low risk
Scans all re-reported

### Outcome measures: Mod risk
Not isolated head trauma- potential for discharge and deterioration

### Confounding Factors: Mod risk
Not isolated head trauma

### Statistical techniques: Mod Risk
Mod risk selective reporting of significant prognostic factors. Does not report whole model.
reviewed by neurosurgeon who determined whether for immediate neurosurgery or conservative management  |  Chronic renal disease $P=1.000$
Renal failure $P=1.000$
ISS score, Median $P=0.005$
Single intracranial haemorrhage $P=0.149$
Multiple intracranial haemorrhage $P=0.149$
EDH $P=0.001$ OR 9.923 95% CI 3.105–31.708
SDH $P=1.000$ OR 0.906 95% CI 0.298–2.753
IPH $P=0.366$ OR 1.812 95% CI 0.594–5.526
SAH $P=0.044$ OR 0.251 95% CI 0.068–0.929
IVH $P=0.111$ OR 13.542 95% CI 1.147–159.876
Midline shift $P=0.001$ OR 19.813 95% CI 5.495–71.435
Skull fracture $P=0.001$ OR 19.813 95% CI 5.495–71.435
Pneumocranium $P=0.621$
Volume of EDH $P=0.092$
Volume of SDH $P=0.657$

Stepwise logistic regression: model included WBC count, midline shift, skull fracture large volume EDH and higher ISS- significant predictors of delayed neurosurgery:

Volume of extra-dural haemorrhage associated with delayed neurosurgery
Increase volume EDH 1 cubic cm increase risk of neurosurgery by 16% ($P=0.022$ OR 1.190 95% CI 1.041–1.362)
AUC volume EDH=0.917 (95% CI 0.797–1.00)

Mean/median GCS=14.7
Mean/median age= 50

| Bardes et al 2016 USA | Level 1 trauma centre West Virginia 2009-2011 | Retrospective Cohort study | Documented neurological decline Medical intervention Neurosurgical intervention | Admissions GCS GCS 6, 12, and 24 hours Type of bleed Bleed progression on CT Aspirin Clopidogrel Warfarin Admission Coag ISS | 389 patients met inclusion criteria 5.1% (20) in hospital mortality 33/389 patients neurological decline 376/389 scheduled repeat CT 69/376 worse CT 35/389 craniotomy 46/389 patients required medical or neurosurgical intervention

Univariate comparison patients with decline versus no neurological decline GCS<15 $P=0.002$
SDH $P=0.0025$
Age$>55$ $P=0.001$
Use Warfarin $P=0.039$
ISS $P=0.22$
AIS$=0$ $P=0.12$
SAH $P=0.15$
EDH $P=0.18$

Study Recruitment: Lod risk Representative sample of population of interest. Limitations of retrospective data collection

Attrition: Low Risk Only inpatient measure

Prognostic factor measurement: Low risk Scans not re-reported

Outcome measures: Mod risk Only inpatient measures- potential for discharge and deterioration

Also some apparent mistakes in univariate analysis

General comments:
Does not report outcomes by single lesion type
ISS<25 Excluded:
- Penetrating injury
- GCS<13
States in results all patients had evidence of intracranial haemorrhage on bleed—doesn’t define what this includes

Decision tree subgroup analysis:
No GCS15 patient ≤ 55 underwent neurological decline= low risk group
Mean/median GCS=14.8
Mean/median age=63
Percent anticoagulated=12

ICB P=0.051
Aspirin P=0.54
Clopidogrel P=0.17
PT P=0.042
aPTT P=0.0028
Admission INR P=0.42

Mean/median GCS=14.8
Mean/median age=63
Percent anticoagulated=12

Sharifuddin et al 2012
Prospective observational study
Aim To evaluate whether the repeat head CT were useful in providing information that leads to any neurosurgical intervention
Repeat CT at 24-48 hours as categorized:
- Unchanged (no change could be assessed based on the size of the injury),
- Improving (resolution or improvement based on the size of the injury)
- Worsened (increase in size or evidence of new intracranial lesion).

Stepwise multiple logistic regression model

Sex
Age (years) ≥ 65 years
Ethnic groups
Mechanism of injury: MVA/Fall/Other
Admission GCS Associated symptoms: Post-traumatic amnesia
Headache
Vomiting
Dizziness
Type of injury identified

279 patients met the inclusion criteria
Neurological decline 66 patients (23.7%)
Worse CT in 58 patients (20.8%).
31 (11.1%) patients neurosurgical outcome.
3 deaths.

Univariate comparison patients with progression on CT and without:
- Male P=0.189
- Age ≥ 65 P = 0.001
- Ethnic groups P=0.624
- Mechanism of injury
- MVA versus others P=0.333
- GCS<15 P=0.003
- Post-traumatic amnesia P=0.069
- Headache P=0.019
- Vomiting P=0.441
- Dizziness P=0.262
- Multiple lesion P=0.001
- Base of skull fracture P=0.865
- Convexity fracture P=0.842
- Hb (g/litre) on admission P=0.009
- INR on admission P=3 0.388

Study Recruitment: Low risk
Retrospective case note review—depends on accuracy of notes.
Not clear if all patients with ICH admitted under neurosurgeon—potential for selection of high risk population. Note age 12+ does not strict meet inclusion criteria.

Attrition: Low Risk
Outcomes only during hospital admission—no loss to F/U

Prognostic factor measurement: Mod risk
The mechanism of injury—doesn’t discriminate between high and low risk mechanisms.
CT interpreted once by attending radiologist or neurosurgeon. No quality control.

Outcome measures: low risk
As reported outcomes of worse CT, neurosurgery or death as an inpatient low risk for bias. However, no follow up outcome measures for delayed deterioration.

Confounding Factors: Mod risk
Not isolated head trauma or control for comorbidities
Does use ISS to exclude severe polytrauma

Statistical techniques: Mod Risk
Mod risk selective reporting of significant prognostic factors.
Does not present decision tree analysis transparently

Sharifuddin et al 2012
Patients admitted under neurosurgeons 2008-2009 specialist centre
Inclusion criteria:
- GCS 13-15
- 12 years and older
- positive initial head CT
- isolated blunt head injury
- presented within 24 hour of initial injury
Excluded:
- previous history of head injury
- on anticoagulation therapy (aspirin, heparin or warfarin)
- polytrauma
- Major comorbidity

Malaysia

Sex
Age (years) ≥ 65 years
Ethnic groups
Mechanism of injury: MVA/Fall/Other
Admission GCS Associated symptoms: Post-traumatic amnesia
Headache
Vomiting
Dizziness
Type of injury identified

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Confounding Factors: Mod risk
Not isolated head trauma or control for comorbidities
Does use ISS to exclude severe polytrauma

Statistical techniques: Mod Risk
Mod risk selective reporting of significant prognostic factors.
Does not present decision tree analysis transparently
### Risk factors for progression on CT:
- **Age ≥ 65** P=0.001  95%C.I. (0.098 - 0.364)
- Multiple lesions on initial CT P=0.018  95% C.I.(0.239 - 0.877)
- GCS score < 15 P= 0.016  95% C.I. (1.164 - 4.333)

### Immediate neurosurgery
- Mean/median GCS=14.6
- Mean/median age= 39
- Percent anticoagulated=0

### Study Recruitment: High risk
- Only recruited patients that neurosurgeons had planned a repeat CT scan (293/442 patients with injuries no repeat CT versus 149/442 for repeat CT)
- Selection bias of higher risk group then all GCS13-15 patients with CT detected injuries

### Attrition: Low Risk
- Outcomes only during hospital admission- no loss to F/U

### Prognostic factor measurement: Mod risk
- No outline of how CT scans reported and risk stratified b

### Outcome measures: low risk
- As reported outcomes of worse CT, neurosurgery or death as an inpatient low risk for bias. However, no follow up outcome measures for delayed deterioration.

### Confounding Factors: Mod risk
- Does not state how patient with other injuries dealt with

### Statistical techniques: Low risk
- Stats do not present what the risk measure is- presumably an OR. Also selective reporting of significant results.

### Patients Admitted to an Acute Care Unit Surgery 2009-2013
- **Inclusion criteria:**
  - Admission<72 hours
  - 16 years and older
  - Non-surgical initial management
  - Includes all GCS score but presents data for GCS13-15 patients
  - Patients under went repeat CT imaging-determined after neurosurgical review

### Retrospective cohort study
- **Aim:** To determine the value of repeat CT imaging in TBI for risk stratification of patients

### Neurologic deterioration: reduced consciousness, limb weakness, lateralizing signs, severe headache, vomiting, and dizziness.

### Neurosurgery
- 145 patients matched inclusion criteria
  - 98/145 GCS13-15
  - 74/98 routine repeated CT scans (36/98 worse)
  - 1/74 neurosurgical

### Overall
- 24/98 clinically deteriorated and underwent CT imaging (7/28 neurosurgery)

### 8/98 GCS13-15 patients neurosurgery
- 24/98 some clinical deterioration-prompting repeat CT

### Univariate comparison patients underwent neurosurgery and did not.
- Age>50 P=0.478
- Mean age P=0.295
- Male P=0.706
- Traffic injury=0.256
- Diabetes mellitus P=0.354
- Hypertension P=0.135
- Ischemic heart disease P=0.070
- Cerebrovascular disease P=0.592
- Aspirin =1.000
- Warfarin P=1.000
- Clopidogrel P=0.017
- ISS, mean p= 0.405
- ISS > 19 P= 0.282
- Brain AIS, mean p=0.080
- AIS > 4 P=0.073
- SBP P=0.240

### Neurosurgery
- 24/98 patients underwent neurosurgery

### Study Recruitment: High risk
- Only recruited patients that neurosurgeons had planned a repeat CT scan (293/442 patients with injuries no repeat CT versus 149/442 for repeat CT)
- Selection bias of higher risk group then all GCS13-15 patients with CT detected injuries
### Study Details

<table>
<thead>
<tr>
<th>Sifri et al 2006</th>
<th>New Jersey Level 1 trauma centre 2002-2003 12 months</th>
</tr>
</thead>
</table>

#### Inclusion criteria:
- Initial GCS 13-15
- Intra-cranial bleed- intra-cerebral, extra-dural, subdural subarachnoid or contusion

#### Excluded:
- Previous brain surgery or cerebral pathology or

#### Prospective Cohort Study

**Aim**
Prospectively assess the value of a repeat CT in patients with mTBI and intra-cranial haemorrhage and normal neurological examination

- Repeat CT within 24 hours
- Neurosurgery following second scan
- Admission to ICU or administration of mannitol following second scan
- In hospital mortality.
- GOS at discharge.
- Discharge destination

**Abnormal neurological examination prior to repeat CT (GCS<15 or severe headache/vomiting/gross motor or sensory deficits)**

- Sex
- Age
- GCS
- Mechanism
- Type of injury identified by CT

#### 161 patients GCS 13-15 with intra-cranial bleed
- 10 excluded due to co-morbidities.
- 5 required immediate neurosurgery
- 16 did not undergo repeat imaging

**130 in study population
- 99 normal neurology at time of repeat CT; 31 abnormal neurology at time of repeat CT.**

**Sex**
- 0/99 neurosurgery
- 1/99 death (unrelated to intra-cranial injury)

**Age**
- 13% 99 CT scans worse
- 2/31 neurosurgery
- 5/31 deaths
- 14/31 repeat CTs worse

**GCS**
- 16/31 repeat CTs worse
- Abnormal neurological exam predicts changes repeat CT OR 5.28 CI 2.08-13.4 P=0.002

**Mean/median GCS=14.6
Mean/median age=45
Percent anticoagulated=4**

**Outcome measures: Mod risk**
Only inpatient related outcome measures.
<table>
<thead>
<tr>
<th>Bee et al 2009</th>
<th>Level 1 trauma centre 2005-2007</th>
<th>Tennessee USA</th>
<th>Excluded:</th>
<th>207 patients met inclusion criteria</th>
<th>Confounding Factors: Mod risk</th>
<th>Cohort includes patients with multiple injuries and abnormal observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria:</td>
<td>Retrospective cohort study</td>
<td>Aim Assess whether repeat CT imaging and ICU admission necessary in mTBI with intra-cranial injury</td>
<td>Percent anticoagulated=0</td>
<td>58/207 worse CT or neurology requiring intervention (4 neurology only)</td>
<td>Statistical techniques: Low Risk</td>
<td>Minimal statistical analysis</td>
</tr>
<tr>
<td>All patients admitted to ICU under neurosurgeon and received a repeat CT scan</td>
<td></td>
<td></td>
<td></td>
<td>31/77 patients multiple/mixed lesions worse CT</td>
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<tr>
<td>Intra-cranial injury CT head</td>
<td></td>
<td></td>
<td></td>
<td>18/207 neurosurgery</td>
<td></td>
<td></td>
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<tr>
<td>Excluded:</td>
<td></td>
<td></td>
<td></td>
<td>2 deaths (1 due to stoke other following craniotomy)</td>
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<tr>
<td>Facial or skull fractures</td>
<td></td>
<td></td>
<td></td>
<td>5/18 neurosurgical= subdurals with no clinical change but worse CT</td>
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<tr>
<td>Immediate neurosurgery</td>
<td></td>
<td></td>
<td></td>
<td><strong>Univariate Comparison</strong> Worsening CT or worsening neurology requiring an intervention versus no deterioration (58 versus 149)</td>
<td></td>
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</tr>
<tr>
<td>Other injuries requiring ICU</td>
<td></td>
<td></td>
<td></td>
<td>Average age worse 47 (47.2 +/- 19.8) No worse 45 (45.5 +/- 18.7) P=0.56</td>
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<td>Average admission SBP worse 152 (152.3 +/- 28.3) No worse 143 (143.1 +/- 25.9) P=0.03</td>
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<td>Average admission pulse worse 87 (86.9 +/- 15.3) No worse 88 (88.5 +/- 16.1) P=0.556</td>
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<td>Average HAIS worse 4.2 (4.21 +/- 0.55) No worse 3.8 (3.84 +/- 0.54) P=0.0001</td>
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<td>Average ISS worse 22.3 (22.3 +/- 6.25) No worse 19.6 (19.6 +/- 6.9) P=0.018</td>
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<td></td>
<td>Mean/median age=46</td>
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</tr>
</tbody>
</table>
Darby MSc Thesis 2015 USA

<table>
<thead>
<tr>
<th>Inclusion criteria:</th>
<th>Retrospective Cohort Study:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial GCS 13-15</td>
<td>To assess whether GCS 15 patients with intra-cranial haemorrhage that maintain a GCS of 15 benefit from routine CT imaging</td>
</tr>
<tr>
<td>Blunt head trauma</td>
<td>Neurosurgical outcomes</td>
</tr>
<tr>
<td>Positive CT scan.</td>
<td>Age/ Age 65 +</td>
</tr>
<tr>
<td>2 or more CT scans</td>
<td>Anti-coagulant</td>
</tr>
<tr>
<td>18+</td>
<td>Medication</td>
</tr>
<tr>
<td>Excluded:</td>
<td>ISS</td>
</tr>
<tr>
<td>Pregnant</td>
<td>LOC</td>
</tr>
<tr>
<td>Age&lt;18</td>
<td>Skull fracture displaced/undisplaced</td>
</tr>
<tr>
<td>Penetrating injury</td>
<td>Neurological symptoms</td>
</tr>
<tr>
<td></td>
<td>Time interval between scans</td>
</tr>
<tr>
<td></td>
<td>GCS/deterioration in GCS</td>
</tr>
</tbody>
</table>

Worse repeat CT imaging 658 patients GCS 13-15 with positive CT scans 88 incomplete notes 201 only 1 CT scan Study population 369 patients with at least 2 CT scans. 111/369 GCS 15 at presentation and throughout. 0/111 neurosurgery 20.7% of 111 worse CT 0.9% mortality 258 GCS<15 at some point during hospital admission 37.6% 258 worse CT 11/258 neurosurgery 2.7% 258 deaths Overall 11/369 neurosurgical interventions

Mean/median age= 53
Progression of Injury:
Unstable GCS < 15 Unadjusted OR 2.21 (95% C.I. 1.33-3.68) adjusted 1.71 (95 % C.I.1.00-2.91) P=0.05
ISS Unadjusted 1.04 (95% C.I. 1.01-1.07) Adjusted 1.1 (0.99-1.05) P=0.27
Age Unadjusted 1.01 (95% C.I. 1.00-1.02) Adjusted 1.01 (0.99-1.02) P=0.08
Anti-coagulation Unadjusted 1.02 (95% CI 0.59-1.77) Adjusted 0.76 (0.40-1.47) P0.42

Risk of Neurosurgery
Unstable GCS unadjusted 4.16 (0.51-33.63) adjusted 2.98 (0.35-25.18) P=0.32
ISS Unadjusted 1.04 (1.01-1.07) adjusted 1.05 (0.99-1.12) P=0.10
Age Unadjusted 1.01 (1.00-1.02) adjusted 1.11 (0.96-1.28)

Fabbri et al 2008 Italian District general hospital rural Italy Prospective cohort study
Aim: Evaluate the follow up GOS at 6 months (includes mortality).
Age, Coagulation status, Charlson Co-morbidity Index, Injury Severity Score
N=718 GCS13-15 patients age>12
Anonymised individual patient made available by authors and used for analysis.

Study Recruitment: High risk
Approximately 1/3 of patients with injuries detected by CT imaging not included either because incomplete or only 1 CT scan.
Patients on which multiple scan conducted likely to be higher risk.

Attrition: Low Risk
Low risk- inpatient outcomes

Prognostic factor measurement: Medium risk
No re-reporting of CTS Does not include CT findings as a prognostic factor.

Outcome measures: Medium risk
No outcome measures after discharge

Confounding Factors: Medium risk
No control for comorbidities

Statistical techniques: Mod Risk
Performs different analysis for neurosurgical outcomes compared to worsening CT scans.
Inclusion criteria:
- Admission GCS score ≥ 9
- Age over 10
- Initial head CT scan positive for any type of trauma
- Initial non-operative management.

Excluded:
- Persistent hypotension caused by additional injuries
- Patients requiring immediate surgery
- Penetrating injuries
- Patients that have been intubated

Effects on outcome of a model based on observation in a neurosurgical unit versus observation in a peripheral hospital with neurosurgical expertise via a teleradiology system and a NSU transfer time of 30–60 min.

Neurosurgical intervention within 7 days.

GCS
CT scan results-
Marshall category
Type of Injury
### Supplementary Material 2: Data Extracted from Included Studies

Papers deriving and validating the BIG criteria N=3 (not included in meta-analysis)

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Study Design</th>
<th>Outcome Measures</th>
<th>Prognostic factors assessed</th>
<th>Results</th>
<th>Quality Appraisal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joseph et al 2014 USA</td>
<td>Level 1 Trauma centre 2009-2011</td>
<td>Retrospective Cohort Study</td>
<td>Neurosurgical intervention Progression of CT findings on a repeated scan</td>
<td>Anticoagulation Anti-platelets OBS on admission to ED GCS Intoxication</td>
<td>1232 patients TBI with positive CT scan 121=BIG 1 313=BIG 2 798=BIG 3 888/1232 underwent repeat CT 13% (159) patients neurological deterioration all in BIG 3 category. No BIG 1 patients had neurological deterioration No Big 1 patient worsening CT 2.6% (9) BIG 2 patients worsening CT 2/313 BIG 2 patients deteriorated neurologically transferred to neurosurgical care No BIG2 patient needed neurosurgery BIG3 patients 21.6% worsening CT 3% neurological deterioration</td>
<td>Study Recruitment: Low risk bias Retrospective cohort review- reliant on accuracy of written notes. Cohort identified by case note review but no details of how this was done- possible selection bias. What constitutes emergent surgical intervention- how many from BIG 1/BIG2 criteria excluded by this. Attrition: low risk Inpatient outcomes only</td>
</tr>
</tbody>
</table>

Inclusion criteria:  
- All TBI patients with CT findings = skull fracture/ICH  
- Transfer or patients requiring emergent surgical intervention  

Exclusion Criteria:  
- Transfer or patients requiring emergent surgical intervention  

Categorisation of these patients into 3 criteria derived through local consensus  

**BIG 1** (discharge after 6 hours obs from ED):  
- GCS 13-15, normal pupils and no focal neurological deficit  
- Not intoxicated  
- Not anti-coagulated or anti-platelets  
- single ICH <5mm and no skull fracture single IPH  

**BIG 2** (admit to hosp not neurosurgeon):  
- GCS 13-15, normal pupils and no focal neurological deficit  
- Can be intoxicated  
- Non-displaced Skull fracture  
- Bleed 5-7mm  
- 2 intra cerebral

Aim:  
- Define guidelines for based patients' history, examination and initial CT head findings regarding which patients require observation in ED, RHCT or neurosurgical consultation.

Local consensus for categories

Progression of CT findings on a repeated scan  
Neurological deterioration if BIG 1 or 2- GCS<12, abnormal focal neurology or abnormal pupils  
CT head scans all reviewed by a single investigator to give size of bleed and associated findings  

Radiology report double checked by one person, only. Definition of neurological deterioration is defined differently as altered mental state and focal deficit and GCS less then 13 in different places.

**Outcome measures:** Mod risk  
No routine follow up of all patients- must re-attend at same hospital to register  

**Confounding Factors:** Low risk  
Age affect outcome and size of bleed  

**Statistical techniques:** N/A
bleeds 3-7mm
- Not anticoagulated or antiplatelets
- BIG 3 (repeat CT and admit under neurosurgeon HDU)
- GCS <13 or abnormal pupils or focal neurological deficit
- Taking anti-coagulant or anti-platelets
- Multiple types of injury on CT
- Bleeds >7mm
- Displaced skull fractures
- Intubated patients

Joseph et al 2014
USA
Study 2 validating the BIG criteria
Identified Search Strategy
March 2012-Dec 2013
Level 1 Trauma centre
Inclusion criteria BIG 1 patients:
- GCS 13-15, normal pupils and no focal neurological deficit
- Not intoxicated
- Not anti-coagulated or anti-platelets
- single ICH <5mm and no skull fracture
- single IPH
Excluded:
- Patients transferred from other hospital
- Intubated
- Patients undergoing emergent

Prospective Cohort Study
Aim To evaluate the established BIG I category for managing patients with traumatic brain injury
Patients remained in ED for observation for 6 hours. If no neurological deterioration discharged.
Repeated neurological assessment every 2 hours if GCS<13, unequal pupils or focal neurological deficit, neurological deterioration
Need for neurosurgical intervention.
Need for Repeat CT due to neurological deterioration.
Hospital or ICU admission.
In-hospital mortality.
30 day readmission

Prospectively recorded:
- Age
- Sex
- Admission observations
- Neurological assessment of GCS, examination and pupils.
- Intoxication
- Anti-platelet or anti-coagulation
- Intubation
- LOC
- Initial CT findings by attending radiologist confirmed by study radiologist
- States 148 patients met criteria prospectively.
- 127/148 patients included and matched 127 patients with matched characteristics of demographics, medications and CT findings before implementation of BIG criteria.
- No patients underwent neurosurgery, had neurological deterioration or died, both of the 127 prospectively recruited and those matched retrospectively.

Study Recruitment: mod risk
States GCS13-15 and range presented as GCS 13-15 but also excludes unexaminable patients and patients with altered mental state- appears cohort does not contain all GCS 14 and 13 patients. Not clear how the cohort was prospectively recruited.

Attrition: mod risk
Disregards 21 of recruited cohort in analysis to match with retrospectively available patients.

Prognostic factor measurement: Mod risk
Reliability of case notes- may be incomplete
The definitions of bleed size are subjective.
Abnormal focal neurology is subjective and clinician dependent. CT scan re-reviewed by a single researcher-possible bias.

Outcome measures: Mod risk
Measures: no structured follow up of every patient.
Patients could have been discharged and died in the community- study would have missed this. States over 50% admitted but that all discharged from the ED in the abstract.
States all patients with TBI prospectively recorded—data not clear how patients identified and recruited. Emergent neurosurgical patients excluded—no definition given |
|----------------------|---------------------------------|-----------------------------|------------------------------------------------------------------------------------------|
| **USA**              | Level 1 Trauma centre           |                             | **Study Recruitment: Low risk**  
States all patients with TBI prospectively recorded—data not clear how patients identified and recruited. Emergent neurosurgical patients excluded—no definition given |
| **Study 2: further validation of BIG criteria** | Inclusion criteria BIG 1 patients:  
- GCS 13-15, normal pupils and no focal neurological deficit  
- Not intoxicated  
- not anti-coagulated or anti-platelets  
- single ICH <5mm and no skull fracture |                             | **Attrition: low risk**  
Outcomes only as inpatients or if re-present |
|                      | Excluded:  
- Transfers  
- Dead on arrival  
- Needed immediate neurosurgery. |                             | **Prognostic factor measurement: Mod risk**  
CT are reviewed by a member of study group—the cut offs are slightly subjective on CT measurement |
|                      | Presents subgroup analysis of BIG 1 patients |                             | **Outcome measures: Mod risk**  
Only measures as inpatient/re-presentation. Potential for discharge and deterioration. |
|                      | Inclusion criteria BIG 1 patients:  
- GCS 13-15, normal pupils and no focal neurological deficit  
- Not intoxicated  
- not anti-coagulated or anti-platelets  
- single ICH <5mm and no skull fracture | Pre BIG  
87 BIG 1/415  
0 neurosurgery  
0 deaths  
3 progression on CT | **Prognostic factor measurement: Mod risk**  
CT are reviewed by a member of study group—the cut offs are slightly subjective on CT measurement |
|                      | Number of routine repeat CT head scans | 68 (78%) admitted  
24 (27.5%) admitted ICU  
76 (87.4%) neurosurgical consultations  
59 (67.8%) repeat CT | **Outcomes only as inpatients or if re-present** |
|                      | Prospective cohort study  
Compare outcomes in TBI before and after implementation of BIG criteria | Pre BIG  
83 BIG 1/381  
0 neurosurgery  
0 deaths  
1 progression on CT | **Prognostic factor measurement: Mod risk**  
CT are reviewed by a member of study group—the cut offs are slightly subjective on CT measurement |
|                      | Neurosurgical consultations  
Progression of bleed on CT | 42 admitted (50.6%)  
6 ICU admission (7.2%)  
7 (8.4%) neurosurgical consultation  
6 (7.2%) repeat CT | **Prognostic factor measurement: Mod risk**  
CT are reviewed by a member of study group—the cut offs are slightly subjective on CT measurement |
|                      | Neurosurgical intervention during hospital admission  
(cranietomy, craniectomy ICP monitoring)  
ICU admission  
30 day readmission | 1 progression on CT | **Outcome measures: Mod risk**  
Only measures as inpatient/re-presentation. Potential for discharge and deterioration. |
|                      | Neurosurgical intervention during hospital admission  
(cranietomy, craniectomy ICP monitoring)  
ICU admission  
30 day readmission | 42 admitted (50.6%)  
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|                      | Neurosurgical intervention during hospital admission  
(cranietomy, craniectomy ICP monitoring)  
ICU admission  
30 day readmission | 1 progression on CT | **Outcome measures: Mod risk**  
Only measures as inpatient/re-presentation. Potential for discharge and deterioration. |

**Unexaminable patients**

- Confounding Factors: Mod risk  
Age not part of BIG1 but could affect outcome and size of bleed  
**Statistical techniques: N/A**  
**General Points:**  
Small numbers of patients in this specific setup. Would support small CT findings low risk, but risk stratification very dependent on accuracy and consistency of radiology report.
Supplementary Material 3: Table of Full Studies Retrieved and Excluded

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<td>Included paediatric patients and patients with no injuries identified by CT imaging</td>
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<td>Chen et al</td>
<td>Uses lumbar puncture to diagnose brain injury</td>
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<td>Included patients of initial GCS&lt;13 Not clear if all GCS13-15 patients have injuries present on CT imaging.</td>
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<td>Zhao et al</td>
<td>Not clear about inclusion criteria and definition of non-operative-no response from authors when contacted.</td>
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<td>Yadav et al</td>
<td>Unable to differentiate initial GCS13-15 patients and included children</td>
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<td>Stein et al \cite{105}</td>
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<td>Innocenti et al \cite{125}</td>
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<td>Muszynski et al \cite{126}</td>
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<td>Patel et al \cite{127}</td>
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<td>Lingsma et al \cite{128}</td>
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<td>Wong et al \cite{129}</td>
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<td>Offner et al \cite{130}</td>
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<td>Bhau et al \cite{132}</td>
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<td>Includes Children and patients without CT identified injuries</td>
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<td>Chieregato et al \cite{116}</td>
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<td>Lesko et al \cite{136}</td>
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<td>68.</td>
<td>Lawrence et al \cite{137}</td>
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<tr>
<td>69.</td>
<td>Roka et al 2008 \cite{119}</td>
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### Supplementary Material 4: Characteristics of included studies

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<th>Size</th>
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### Supplementary Material 5: Table of Risk Factors Assessed

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Supplementary Material 6: Forest plots of within study risk factors’ effect on the risk of neurosurgery or clinical deterioration

Meta-analysis of effect of initial GCS=15 on Risk of Clinical Deterioration/Neurosurgery

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<td>17.3%</td>
<td>0.28</td>
<td>[0.14, 0.54]</td>
</tr>
<tr>
<td>Schindler et al 2016</td>
<td>66</td>
<td>129</td>
<td>57</td>
<td>23.7%</td>
<td>0.35</td>
<td>[0.23, 0.52]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1682</td>
<td>631</td>
<td>1682</td>
<td>100.0%</td>
<td>0.35</td>
<td>[0.23, 0.52]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.13, Chi² = 10.65, df = 4 (P = 0.03), I² = 62%
Test for overall effect: Z = 5.16 (P < 0.00001)

Meta-analysis effect of isolated Subarachnoid haemorrhage versus any other injury on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Isolated SAH</th>
<th>Any Other Injury Type</th>
<th>Total Events</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borzutzky et al 2013</td>
<td>1</td>
<td>76</td>
<td>47</td>
<td>328</td>
<td>14.2%</td>
<td>0.08 [0.01, 0.59]</td>
</tr>
<tr>
<td>Pruett et al 2016 (neurosurg.)</td>
<td>0</td>
<td>4</td>
<td>155</td>
<td>216</td>
<td>8.2%</td>
<td>0.15 [0.01, 2.84]</td>
</tr>
<tr>
<td>Schindler et al 2016</td>
<td>27</td>
<td>57</td>
<td>96</td>
<td>144</td>
<td>32.3%</td>
<td>0.45 [0.24, 0.84]</td>
</tr>
<tr>
<td>Sweeney et al 2015 (neurosurg.)</td>
<td>197</td>
<td>4315</td>
<td>37305</td>
<td>37.2%</td>
<td>0.12</td>
<td>[0.08, 0.13]</td>
</tr>
<tr>
<td>Veerman et al 2006 (neurosurg.)</td>
<td>0</td>
<td>28</td>
<td>44</td>
<td>121</td>
<td>8.2%</td>
<td>0.39 [0.02, 7.42]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>13512</td>
<td>36141</td>
<td>13512</td>
<td>100.0%</td>
<td>0.19</td>
<td>[0.07, 0.50]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.63, Chi² = 19.78, df = 4 (P = 0.001), I² = 78%
Test for overall effect: Z = 3.39 (P = 0.00007)

Meta-analysis effect of Isolated Extradural versus any other injury on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Isolated EDH</th>
<th>Any Other Injury Type</th>
<th>Total Events</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borzutzky et al 2013</td>
<td>0</td>
<td>4</td>
<td>47</td>
<td>387</td>
<td>0.3%</td>
<td>2.64 [0.11, 85.82]</td>
</tr>
<tr>
<td>Pruett et al 2016 (neurosurg.)</td>
<td>0</td>
<td>5</td>
<td>366</td>
<td>366</td>
<td>0.3%</td>
<td>7.32 [0.35, 153.20]</td>
</tr>
<tr>
<td>Schindler et al 2016</td>
<td>1</td>
<td>122</td>
<td>200</td>
<td>192</td>
<td>0.3%</td>
<td>1.92 [0.08, 47.79]</td>
</tr>
<tr>
<td>Sweeney et al 2015 (neurosurg.)</td>
<td>159</td>
<td>4316</td>
<td>49595</td>
<td>98.8%</td>
<td>0.92</td>
<td>[0.88, 2.56]</td>
</tr>
<tr>
<td>Veerman et al 2006 (neurosurg.)</td>
<td>0</td>
<td>7</td>
<td>144</td>
<td>121</td>
<td>8.2%</td>
<td>2.08 [0.10, 43.34]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>915</td>
<td>50683</td>
<td>50683</td>
<td>100.0%</td>
<td>2.26</td>
<td>[1.90, 2.68]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00, Chi² = 0.60, df = 4 (P = 0.96), I² = 0%
Test for overall effect: Z = 9.22 (P = 0.00001)

Meta-analysis Isolated subdural versus any other Injury on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Isolated Subdural</th>
<th>Any Other Injury Type</th>
<th>Total Events</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borzutzky et al 2013</td>
<td>24</td>
<td>160</td>
<td>244</td>
<td>244</td>
<td>26.4%</td>
<td>1.62 [0.68, 3.86]</td>
</tr>
<tr>
<td>Pruett et al 2016 (neurosurg.)</td>
<td>4</td>
<td>161</td>
<td>210</td>
<td>210</td>
<td>7.9%</td>
<td>12.03 [0.64, 225.05]</td>
</tr>
<tr>
<td>Schindler et al 2016</td>
<td>18</td>
<td>36</td>
<td>105</td>
<td>165</td>
<td>25.2%</td>
<td>0.57 [0.28, 1.18]</td>
</tr>
<tr>
<td>Sweeney et al 2015 (neurosurg.)</td>
<td>2977</td>
<td>18784</td>
<td>31712</td>
<td>29.4%</td>
<td>3.80</td>
<td>[3.58, 4.08]</td>
</tr>
<tr>
<td>Veerman et al 2006 (neurosurg.)</td>
<td>3</td>
<td>110</td>
<td>44</td>
<td>44</td>
<td>11.1%</td>
<td>1.21 [0.12, 11.91]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>19351</td>
<td>32375</td>
<td>32375</td>
<td>100.0%</td>
<td>1.82</td>
<td>[0.69, 4.77]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.62, Chi² = 34.90, df = 4 (P = 0.00001), I² = 89%
Test for overall effect: Z = 1.21 (P = 0.23)
Meta-analysis Isolated contusion versus any other Injury on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Isolated Contusion Events</th>
<th>Any Other Injury Type Events</th>
<th>Total Events</th>
<th>Total Weight IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borczuk et al 2013</td>
<td>2</td>
<td>33</td>
<td>46</td>
<td>271.0%</td>
<td>0.32 [0.07, 1.37]</td>
</tr>
<tr>
<td>Prift et al 2016</td>
<td>0</td>
<td>20</td>
<td>4</td>
<td>341.0%</td>
<td>1.23 [0.60, 2.30]</td>
</tr>
<tr>
<td>Sweeney et al 2015</td>
<td>139</td>
<td>5636</td>
<td>4335</td>
<td>44860.98%</td>
<td>0.24 [0.20, 0.28]</td>
</tr>
<tr>
<td>Total (95%) CI</td>
<td>5699</td>
<td>45472</td>
<td>4395</td>
<td>100.0%</td>
<td>0.24 [0.20, 0.28]</td>
</tr>
</tbody>
</table>

Total events 141 4395

Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.34, df = 2 (P = 0.51); P = 0
Test for overall effect Z = 16.54 (P = 0.00001)

Meta-analysis of effect of coagulopathy use on Clinical Deterioration/Neurosurgery:

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Anti-coagulated Events</th>
<th>Not Anti-coagulated Events</th>
<th>Total Events</th>
<th>Total Weight IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barons et al 2016</td>
<td>200</td>
<td>400</td>
<td>600</td>
<td>120.0%</td>
<td>0.72 [0.57, 0.90]</td>
</tr>
<tr>
<td>Borczuk et al 2013</td>
<td>150</td>
<td>350</td>
<td>500</td>
<td>100.0%</td>
<td>0.77 [0.61, 0.99]</td>
</tr>
<tr>
<td>Kim et al 2014</td>
<td>50</td>
<td>250</td>
<td>300</td>
<td>60.0%</td>
<td>0.98 [0.86, 1.12]</td>
</tr>
<tr>
<td>Shih et al 2016</td>
<td>100</td>
<td>200</td>
<td>300</td>
<td>60.0%</td>
<td>0.85 [0.74, 0.99]</td>
</tr>
<tr>
<td>Total (95%) CI</td>
<td>2400</td>
<td>5000</td>
<td>7400</td>
<td>100.0%</td>
<td>0.95 [0.86, 1.05]</td>
</tr>
</tbody>
</table>

Total events 2000 7400

Heterogeneity: Tau^2 = 0.00; Chi^2 = 7.22, df = 7 (P = 0.37); P = 0
Test for overall effect Z = 2.24 (P = 0.025)

Meta-analysis effect of aspirin/anti-platelet use on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>No anti-platelet Events</th>
<th>Anti-platelet Events</th>
<th>Total Events</th>
<th>Total Weight IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barons et al 2016</td>
<td>200</td>
<td>200</td>
<td>400</td>
<td>100.0%</td>
<td>0.78 [0.67, 0.91]</td>
</tr>
<tr>
<td>Borczuk et al 2013</td>
<td>130</td>
<td>220</td>
<td>350</td>
<td>100.0%</td>
<td>0.86 [0.75, 0.99]</td>
</tr>
<tr>
<td>Kim et al 2014</td>
<td>30</td>
<td>220</td>
<td>250</td>
<td>50.0%</td>
<td>0.94 [0.85, 1.04]</td>
</tr>
<tr>
<td>Shih et al 2016</td>
<td>100</td>
<td>200</td>
<td>300</td>
<td>60.0%</td>
<td>0.89 [0.79, 0.99]</td>
</tr>
<tr>
<td>Total (95%) CI</td>
<td>410</td>
<td>310</td>
<td>720</td>
<td>100.0%</td>
<td>0.90 [0.81, 1.00]</td>
</tr>
</tbody>
</table>

Total events 710 720

Heterogeneity: Tau^2 = 0.00; Chi^2 = 7.22, df = 7 (P = 0.37); P = 0
Test for overall effect Z = 2.24 (P = 0.025)

Meta-analysis effect of clopidogrel/anti-platelet use on Clinical Deterioration/Neurosurgery

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Anti-platelet Events</th>
<th>No Anti-platelet Events</th>
<th>Total Events</th>
<th>Total Weight IV, Random, 95% CI</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barons et al 2016</td>
<td>200</td>
<td>200</td>
<td>400</td>
<td>100.0%</td>
<td>0.78 [0.67, 0.91]</td>
</tr>
<tr>
<td>Borczuk et al 2013</td>
<td>140</td>
<td>260</td>
<td>400</td>
<td>120.0%</td>
<td>0.92 [0.81, 1.03]</td>
</tr>
<tr>
<td>Kim et al 2014</td>
<td>100</td>
<td>200</td>
<td>300</td>
<td>60.0%</td>
<td>0.88 [0.78, 0.99]</td>
</tr>
<tr>
<td>Nishimizu et al 2014</td>
<td>100</td>
<td>200</td>
<td>300</td>
<td>60.0%</td>
<td>0.88 [0.78, 0.99]</td>
</tr>
<tr>
<td>Total (95%) CI</td>
<td>410</td>
<td>310</td>
<td>720</td>
<td>100.0%</td>
<td>0.90 [0.81, 1.00]</td>
</tr>
</tbody>
</table>

Total events 710 720

Heterogeneity: Tau^2 = 0.00; Chi^2 = 7.22, df = 7 (P = 0.37); P = 0
Test for overall effect Z = 2.24 (P = 0.025)
Supplementary Material 7: Pooled risk of clinical deterioration stratified by the injury type identified by initial CT imaging