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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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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 GCS13, 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 GCS13-15 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 GCS13-15. 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 GCS13-15 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 heterogenous 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"?

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

1. Perel, P., Edwards, P., Wentz, R. and Roberts, I. (2006). Systematic review of prognostic models in traumatic brain injury. BMC Med Inform Decis Mak 6, 38.

The risk of deterioration in ~~CT identified~~ GCS13-15 patients with traumatic brain injury identified by CT imaging~~mild Traumatic Brain Injur y~~. 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~~ery~~ 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~~ery~~ 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~~ery~~ 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 m~~M~~any studies' was~~ere~~ 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~~the~~ prognostic factors; ~~r~~Research is needed to derive and a validate a usable clinical decision rule so that~~before~~ 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.[1, 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~~ery~~ 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]

Other~~s~~ 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,~~-~~ have been useful in predicting adverse outcomes in patients with more severe TBI, but they are not applicable to this patient group ~~are not applicable to this 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~~that~~ 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.[14] 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~~ery~~ 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.[5]

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. [1, 3, 10, 15-17 18 19, 20] 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.[21] 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).[22] The Freeman-Tukey double arscine transformation was used to include studies with no adverse outcomes and a random effects model was used due to study heterogeneity.[23]

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).[24, 25] The log odds of clinical deterioration, ~~neurosurgery~~neurosurgical intervention 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.[26] A Random Effects model was used due to the heterogeneity of study populations, prognostic factor and outcome measures.[23] 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[6, 9, 27-93] and 2 reviews[19, 20] were retrieved. A "grey" literature search identified a further 129 studies for title and abstract screening of which 3 were retrieved.[94-96]

Reference and citation searching of included studies and selected reviews and guidelines identified another 46 studies[7, 8, 39, 97-139] for full retrieval and 3 additional systematic reviews[17, 18, 140] 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. [6-9, 27, 28, 30, 32, 37, 41, 42, 52, 54, 55, 57, 59, 60, 62, 63, 65, 66, 69, 71, 73-78, 86, 87, 90, 93, 97-104, 106-109, 114, 125, 130, 139] One review presented new study data.[18] The 4 remaining reviews formed part of the narrative synthesis. [17, 19, 20, 140] 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.[139]

Study Characteristics

Supplementary material 4 presents the characteristics of included studies. Seven prospective studies were identified[28, 66, 74, 75, 90, 114, 139] and 4 studies had a sample size of over 1000.[63, 87, 98, 108] Forty-six studies estimated the outcomes of interest and contribute to pooled estimates of risk.[6-9, 27, 28, 30, 32, 37, 41, 42, 52, 54, 55, 57, 59, 60, 62, 63, 65, 66, 69, 71, 73-78, 86, 87, 90, 93, 97-104, 106-109, 114, 125, 130, 139] Four studies present data regarding specific injury sub-types.[32, 55, 71, 103] One study only contributes to the narrative synthesis

due to the outcome measure it assessed.[42] Three studies present the Brain Injury Guidelines (BIG) risk stratification tool.[9, 27, 109] 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.[6, 37, 41, 54, 55, 66, 69, 71, 73-78, 87, 98-101, 130, 139] Sixteen studies present multi-variable models using logistic regression or recursive partitioning.[6, 37, 41, 54, 55, 66, 69, 71, 73, 74, 77, 78, 98, 100, 101, 130] Only 2 studies attempted to validate such models by splitting the study data sets.[66, 98]

Quality Assessment

QUIPS quality scores are presented in supplementary material 2.[21] The following common methodological issues were identified.

Study recruitment was often ~~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.[7, 18, 54, 74-78, 86, 90, 102, 104, 106, 107, 125, 130] Even when re-imaging was presented as routine practice, it was often indicated that not all patients were re-imaged and included in analysis.[6] 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.[37]

In 32 studies outcomes were assessed during inpatient admission and so patients who were discharged and deteriorated were missed. In other studies, is 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.[66] Other studies indicated some recorded deaths were related to comorbidities instead of TBI.[41, 73]

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

Death

Twenty-seven studies assessed the outcome of death.[6, 8, 28, 41, 52, 57, 60, 62, 63, 65, 69, 73-75, 78, 86, 93, 97, 99-102, 104, 114, 125, 130 139] 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%C.I. 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.[6-9, 27, 30, 37, 52, 54, 57, 60, 62, 63, 65, 66, 73-78, 86, 90, 93, 97-102, 104, 106, 109, 114, 125, 130, 139] 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 ~~neurosurgery~~neurosurgical intervention reported by Beynon et al[93] 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 ~~neurosurgery~~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 ~~neurosurgery~~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 ~~neurosurgery~~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 ~~neurosurgery~~neurosurgical intervention.[8, 52, 62, 106] This is explained by:

exclusion of anti-coagulated patients,[8, 52, 62] selection of patients for non-ICU admission or other reduced other care pathays,[8, 52, 62] and exclusion of patients with large injuries[8].

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 ~~neurosurgery~~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.[8, 37, 41, 63, 66, 69, 73, 74, 76-78, 100, 101, 104, 107, 108, 114, 125] 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. [6, 18, 27, 28, 30, 41, 62, 74-78, 87, 90, 97, 99-102, 104, 106-108, 114, 125, 130] 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.[6, 37, 41, 54, 55, 66, 69, 71, 73-78, 87, 98-101, 130, 139] 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.[6, 37, 41, 54, 55, 66, 69, 71, 73, 74, 76-78, 98-101, 130] Ten studies[37, 41, 54, 66, 73, 74, 76-78, 101] assessed age using 4 different dichotomous cut offs and 11 studies measured age as a continuous factor. [6, 55, 69, 71, 73, 76, 77, 98-100, 130] 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.[69, 71, 98, 130] However, in 4 of 6 multivariable models where it was dichotomised, older age predicted the outcomes of interest. [41, 54, 66, 73, 78, 101] 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.[6, 37, 41, 55, 66, 69, 73, 74, 77, 98, 100, 101] 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). [37, 41, 66, 73, 74, 77, 101] Two papers assessed progression of injury on repeat CT imaging and both found initial GCS 15 to be associated with reduced risk of progression.[74, 77] Four studies estimated the effect of an initial GCS of 15 in multivariable models.[37, 66, 73, 101] All 4 multi-variable 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.[6, 41, 54, 55, 66, 73, 76, 78, 100] 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, 66] The Marshall classification was assessed as a continuous[73] 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 ~~neurosurgery~~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: ~~neurosurgery~~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 ~~neurosurgery~~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 multi-variable 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 ~~neurosurgery~~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%) ~~neurosurgery~~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 ~~neurosurgery~~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 ~~neurosurgery~~neurosurgical intervention/clinical deterioration (Table 2). In multivariable meta-regression, a unit increase in mean/median study population GCS was associated with an 0.12 reduction in the odds of ~~neurosurgery~~neurosurgical intervention (Table 1). Pooling of univariable models indicated that patients with initial GCS~~<~~15 had odds of clinical deterioration/~~neurosurgery~~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).[150] 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.[141] 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.[142]

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.[13, 143]

Context

When the Canadian CT Head Rule was developed, the authors presented a consensus derived list of intra-cranial injuries that would never require ~~neurosurgery~~neurosurgical intervention.[4] The implication was that patients with such injuries were safe for discharge. This was rejected by the Society of British Neurological Surgeons.[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.[109] They propose such patients are safe for discharge after 6 hours of ED observation.[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.[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.[108] 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 ~~mTBI~~ 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.[6, 78] 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.[17-20]

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.[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 heterogenous 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.

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

Factor	Outcome	Unit Increase Affect Odds Univariable Model	Unit Increase Affect Odds Multivariable Model
Mean Age Study Population	Death	1.05 (95% C.I. 1.0003-1.12) P= 0.049	1.06 (95% C.I. 1.0002-1.12) P= 0.049
Mean GCS Study Population	Death	0.12 (95% C.I. 0.02- 0.86) P=0.04	0.09 (95% C.I. 0.01- 0.59) P=0.02
Lower risk study population versus ICU population	Death	0.27 (95% C.I. 0.08-0.94) P=0.04	
Unselected study population versus ICU population	Death	0.81 (95% C.I. 0.22-1.97) P=0.63	
Percentage population Anticoagulated	Death	1.05 (95% C.I. 0.95-1.17) P=0.32	
Mean Age Study Population	Neurosurgery	1.01 (95% C.I. 1.02- 1.11) P=0.01	1.09 (95% C.I. 1.02-1.16) P=0.02
Mean GCS Study Population	Neurosurgery	0.71 (95% 0.01- 0.56) P=0.01	0.12 (95% C.I. 0.02- 0.91) P=0.04
Lower risk study population versus ICU population	Neurosurgery	0.13 (95% C.I. 0.04- 0.41) P<0.01	0.67 (95% C.I. 0.10- 4.37) P=0.66
Unselected study population versus ICU population	Neurosurgery	0.95 (95% C.I. 0.43- 2.12) P=0.90	1.34 (95% C.I. 0.45-4.02) P=0.58
Percentage population	Neurosurgery	1.1 (95% C.I. 1.01-1.19) P=0.04	

Anticoagulated			
Exclusion of anti-coagulated patients in study selection	Neurosurgery	0.63 (95% C.I. 0.27- 1.43) P=0.26	1.33 (95% C.I. 0.51- 3.49) P=0.54
Mean Age Study Population	Clinical Deterioration	1.01 (95% C.I. 0.95-1.09) P=0.64	1.02 (95% C.I. 0.93-1.12) P=0.59
Mean GCS Study Population	Clinical Deterioration	0.36 (95% C.I. 0.04-3.20) P=0.33	0.26 (95% C.I. 0.02-3.76) P=0.29

Table 2: Summary of effect estimates of risk factors assessed within studies

Risk Factor	Number of Studies Assessed in	Pooled Univariable Effect*	Effect Multi-variable Models**	Likely Effect on Risk
Age	18[6, 37, 41, 54, 55, 66, 69, 71, 73, 74, 76-78, 98-101, 130]		+6/11	+
Initial GCS 15	7[37, 41, 66, 73, 74, 77, 101]	OR 0.35 95% CI: 0.23 to 0.52	- 4/4	-
Severity CT brain	9[6, 41, 54, 55, 66, 73, 76, 78, 100]		+7/8	+
Isolated SAH	5[37, 73, 77, 98, 108]	OR 0.19 95% CI: 0.07 to 0.5	-1/2	-
Isolated EDH	5[37, 73, 77, 98, 108]	OR 2.26 95% CI: 1.9 to 2.68	+1/1	+
Isolated SDH	5[37, 73, 77, 98, 108]	OR 1.82 95% CI: 0.69 to 4.77	+2/2	
Isolated Contusion	3[37, 98, 108]	OR 0.24 95% CI: 0.2-0.28	0/1	
Anti-coagulation	12[6, 37, 41, 55, 74, 76-78, 98, 100, 101, 139]	OR 1.45 95% CI: 1.28-1.64	0/2	+
Aspirin	6[37, 55, 66, 76, 87, 101]	OR 1.30 95% CI: 0.95-1.78		
Clopidogrel	6[37, 55, 66, 76, 87, 101]	OR 1.79 95% CI:1.17-2.72		+

*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

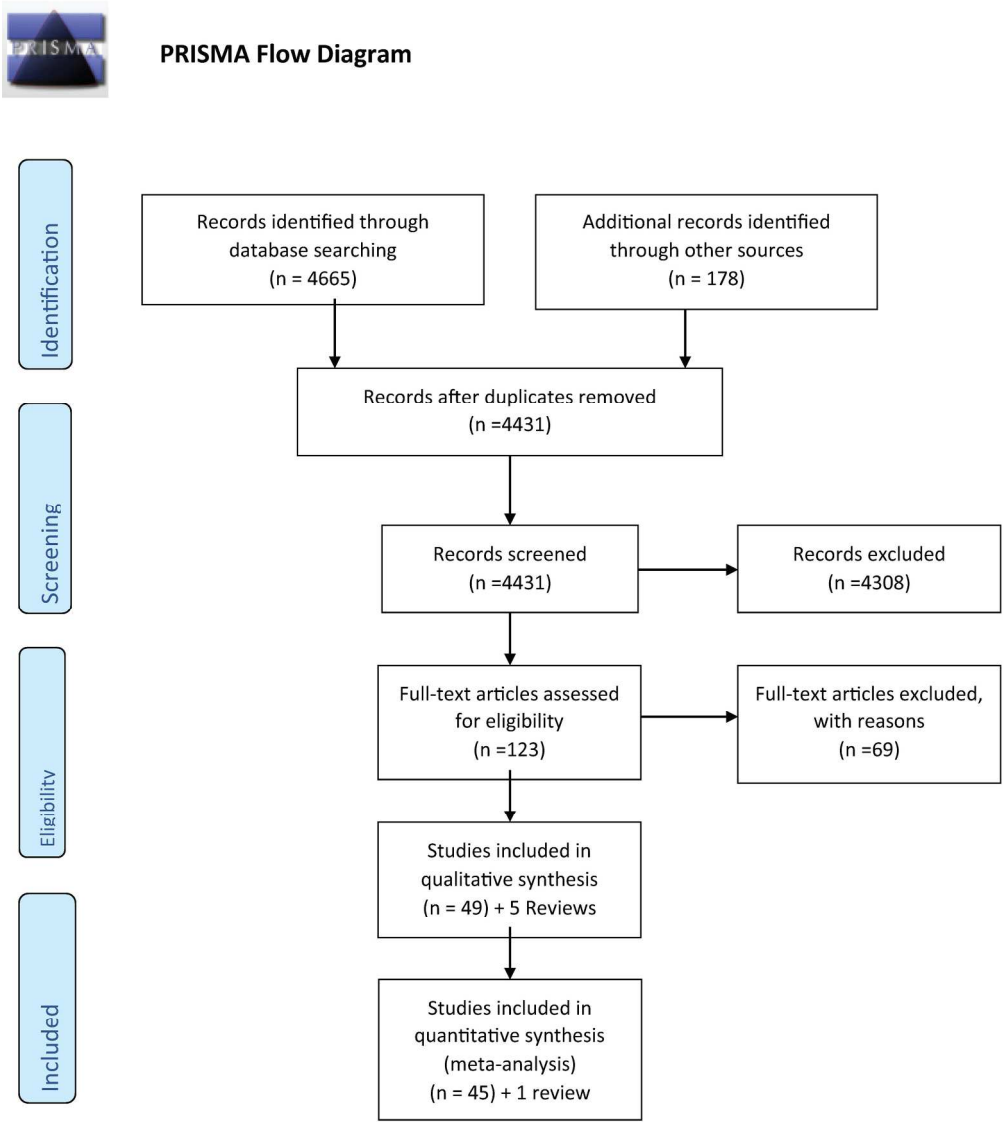

Figure 1

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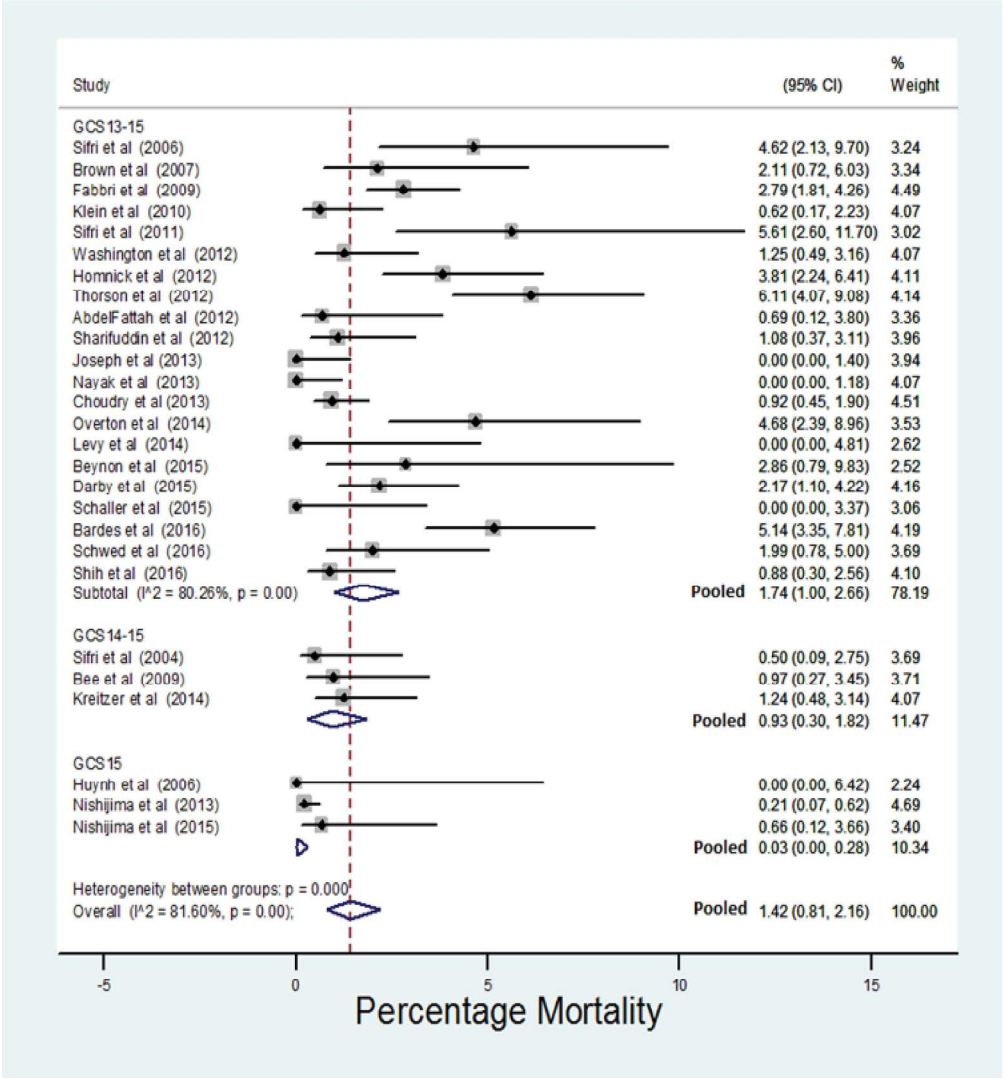

Figure 2

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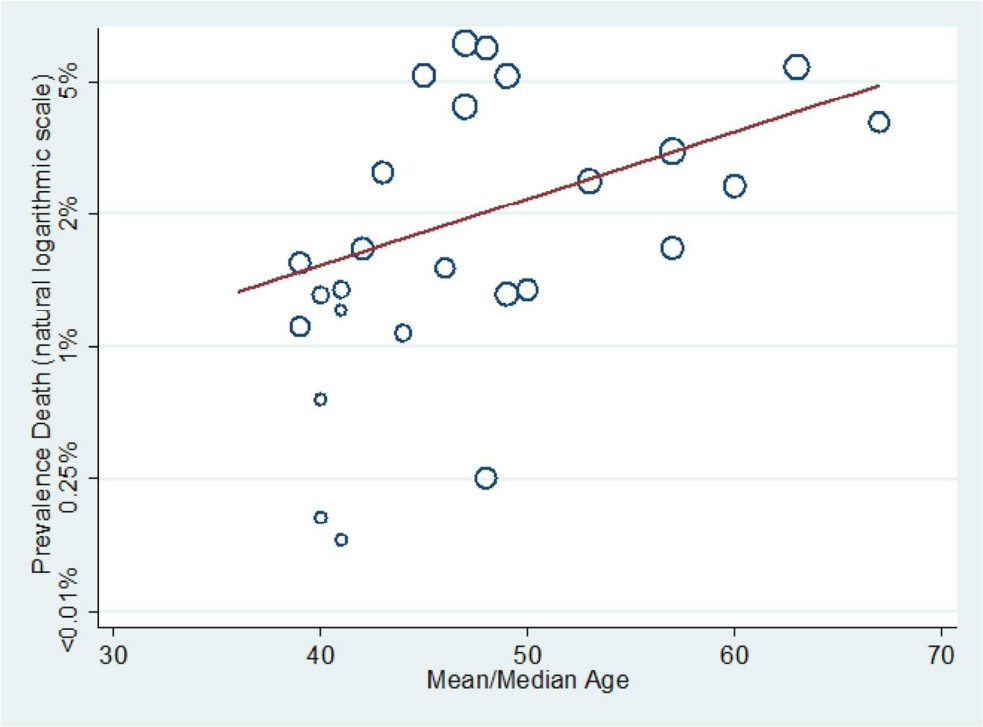

Figure 3

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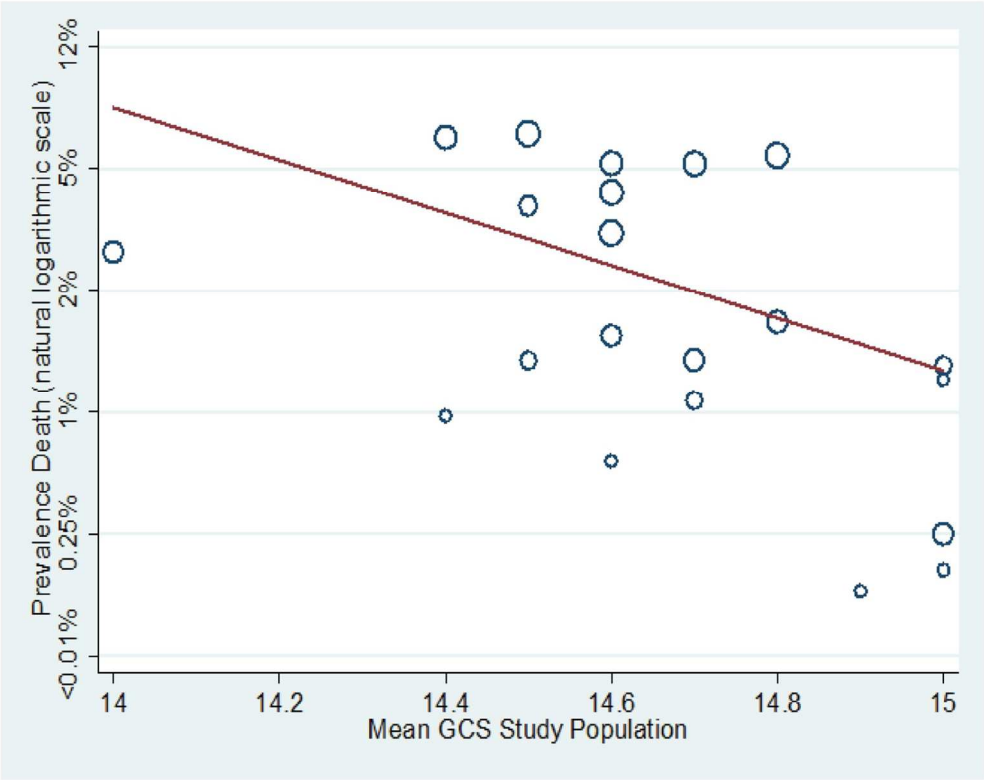

Figure 4

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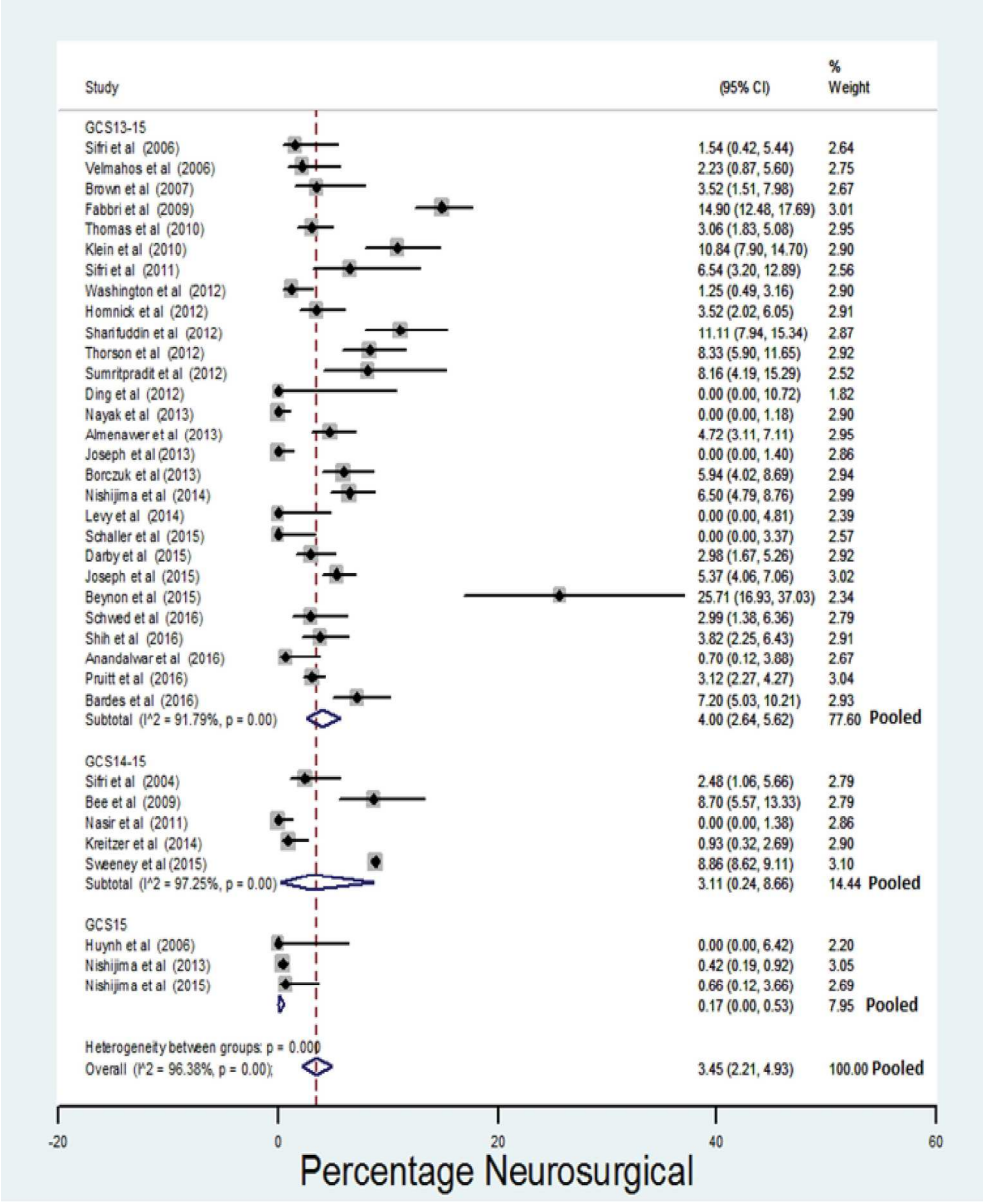

Figure 5

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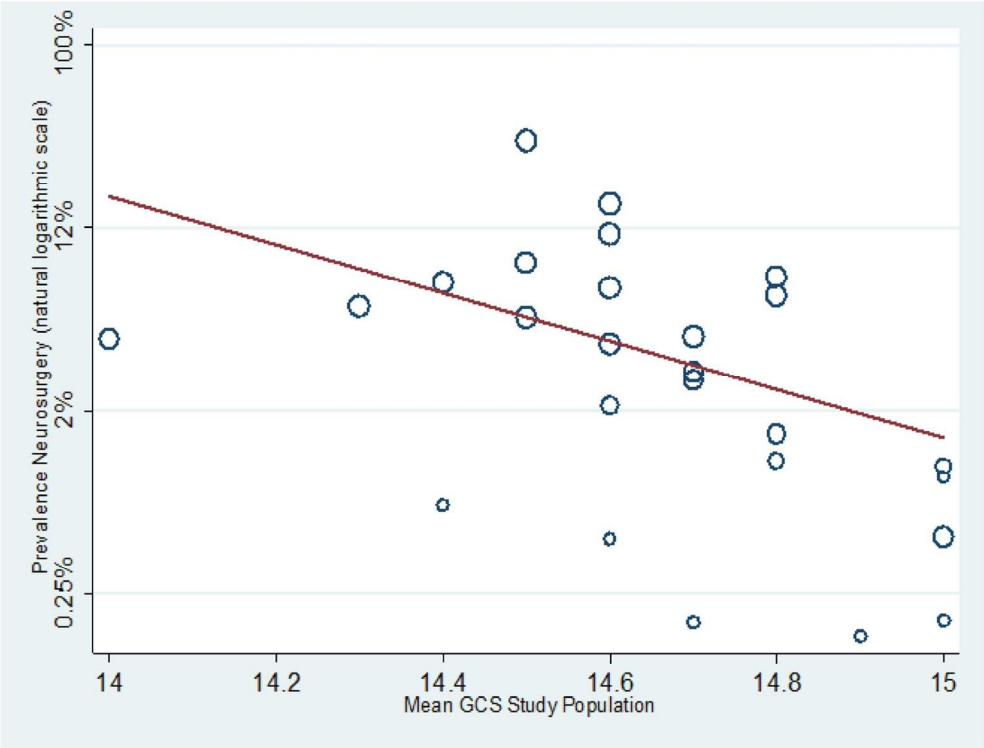

Figure 6

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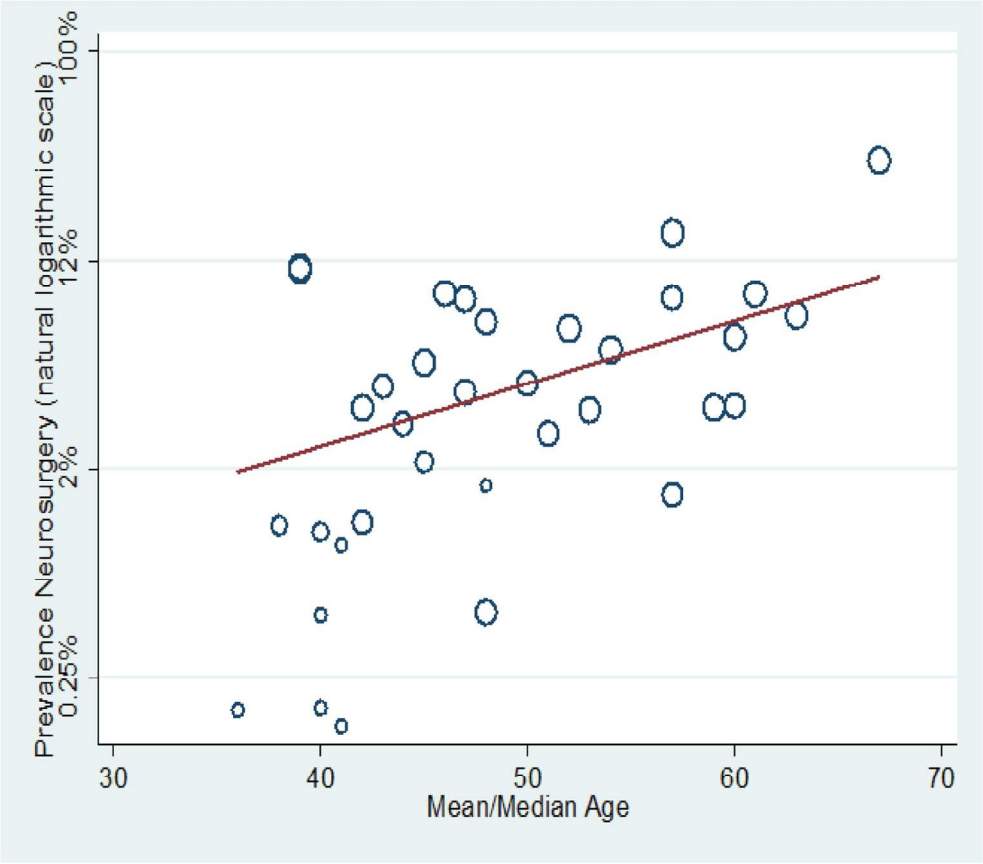

Figure 7

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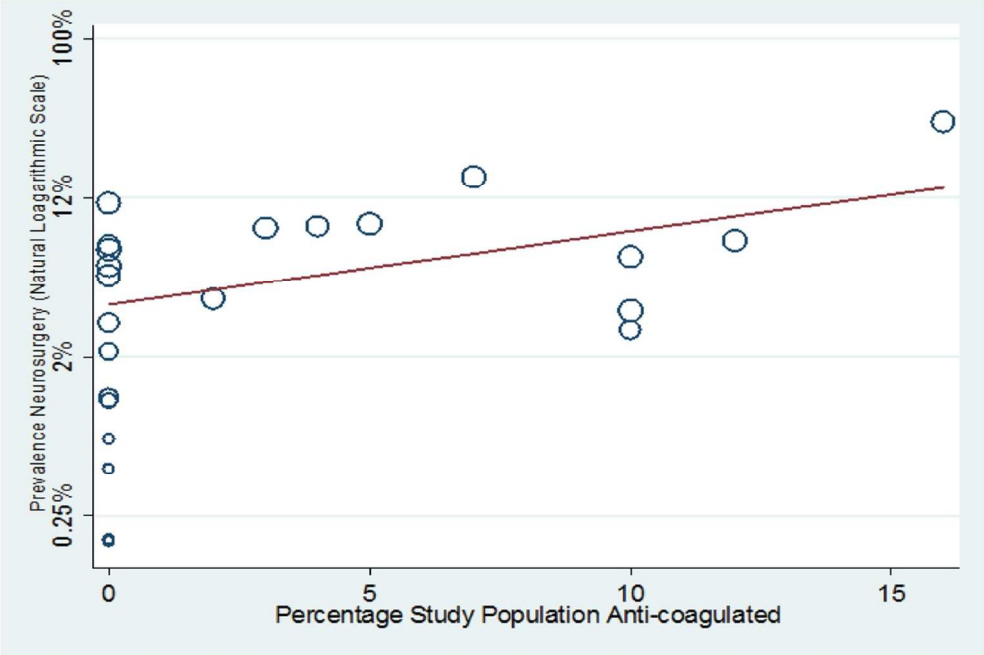

Figure 8

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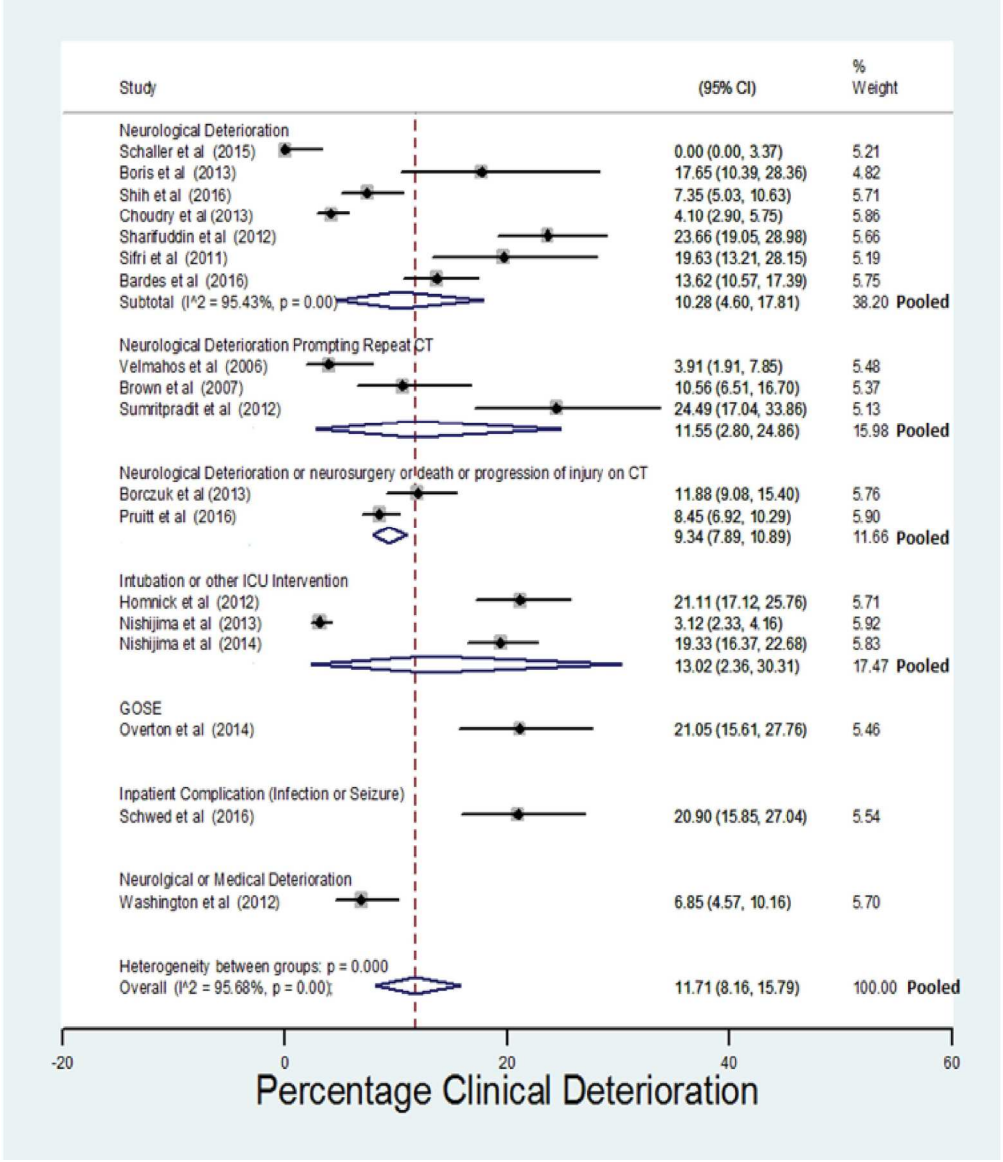

Figure 9

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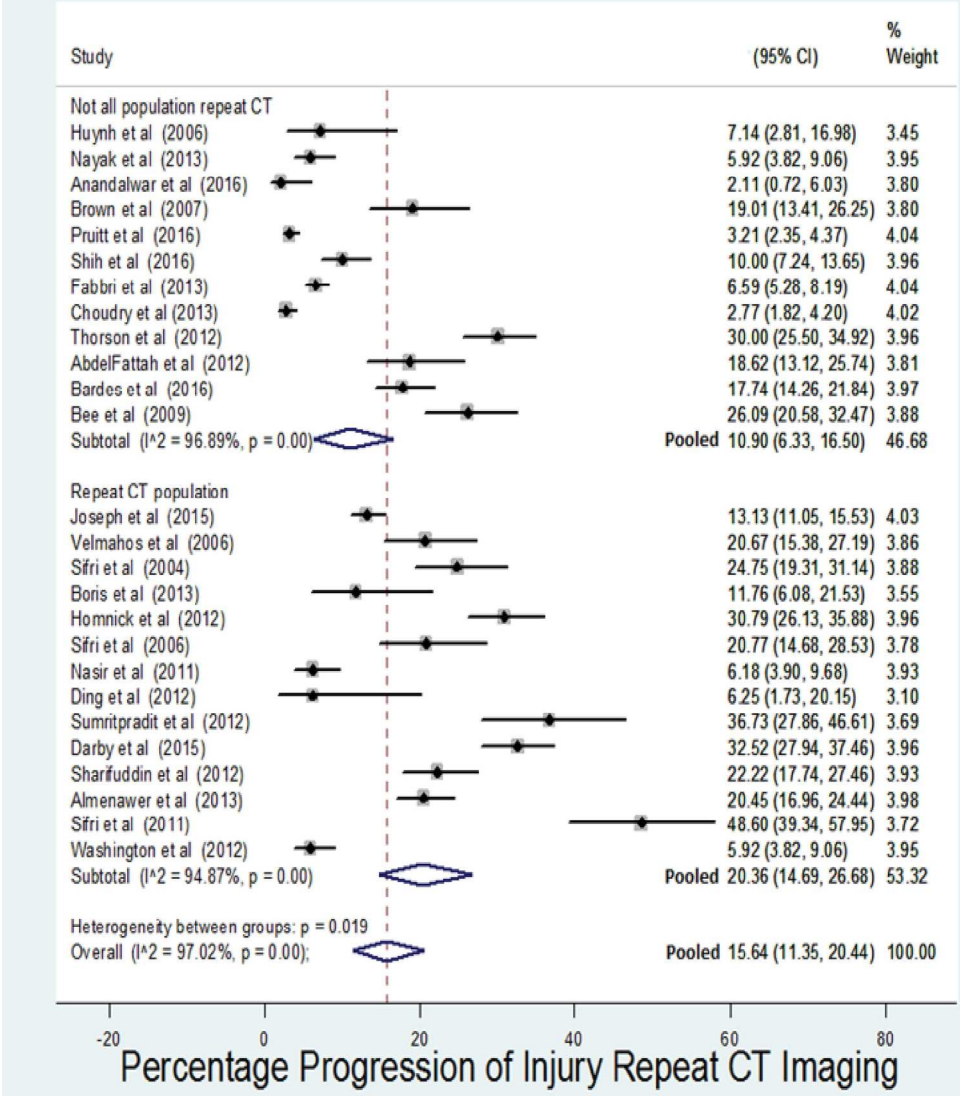

Figure 10

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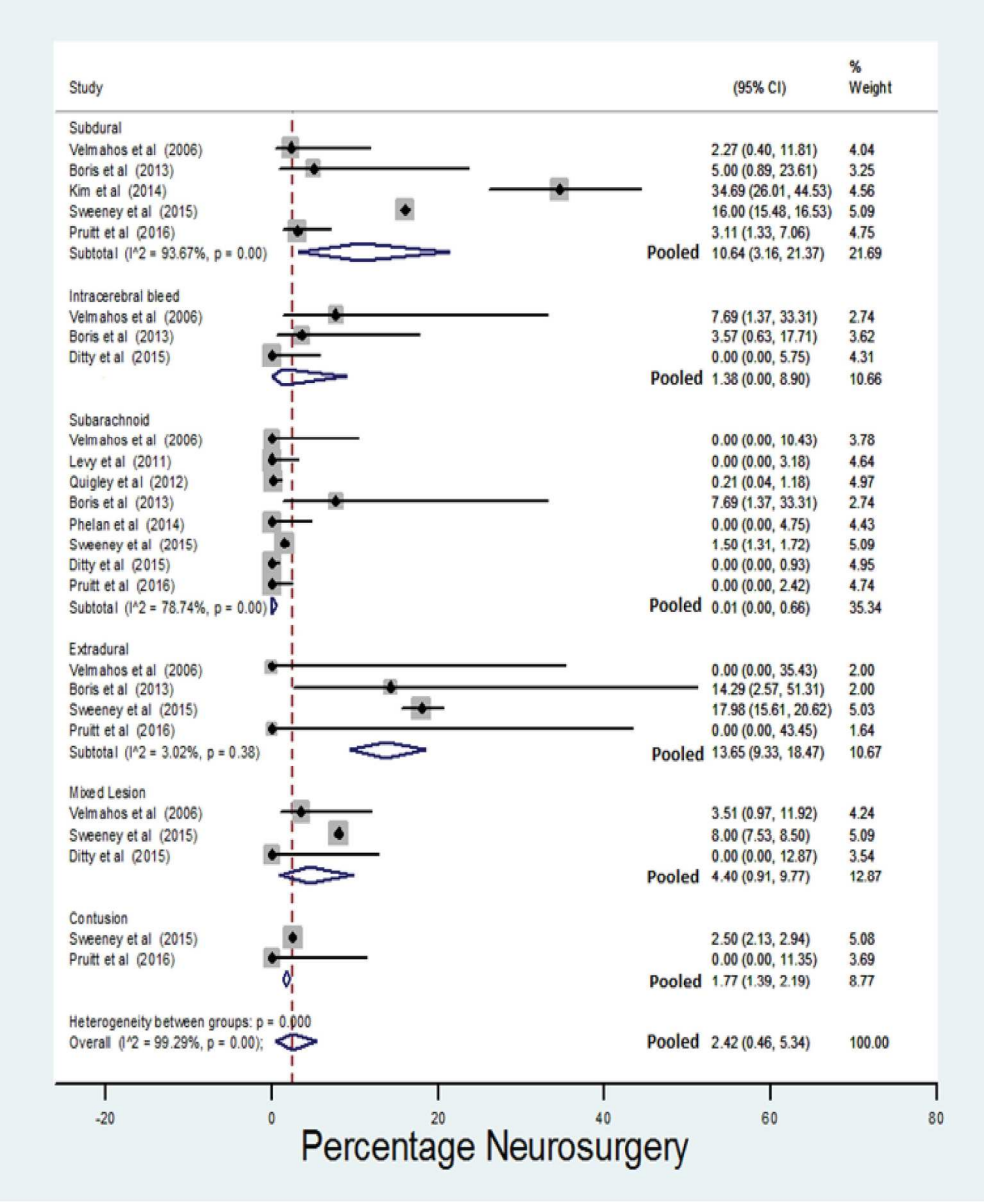


Figure 11

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% 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:

12	1 and 10 and 11	3167
11	2 or 3 or 4 or 5 or 6 or 9	104649
10	7 or 8	2298555
9	"cerebral contusion".mp. or exp brain contusion/	2627
8	exp outcome variable/ or outcome.mp. or exp critical care outcome/ or exp adverse outcome/	1787765
7	exp prognosis/ or prognos*.mp.	704898
6	exp subarachnoid hemorrhage/ or "traumatic subarachnoid h#em*".mp.	28977
5	"extradural h#em*".mp.	225
4	exp epidural hematoma/ or "epidural h#em*".mp.	4775
3	exp subdural hematoma/ or "subdural h#em*".mp.	10281
2	exp Intracranial Hemorrhages/ or "intracranial h#em*".mp.	92720
1	"traumatic brain injury".mp. or traumatic brain injury/ or head injury/	69888

MEDLINE **Ovid MEDLINE(R) without Revisions** 1996 to November Week 3 2016

24/11/2016

9	1 and 7 and 8	1143
8	2 or 3 or 4 or 5 or 6	34984
7	exp Risk Factors/ or risk.mp. or exp Risk/ or exp Risk Assessment/	1502469
6	"traumatic subarachnoid h#emorrhage".mp. or exp Subarachnoid Hemorrhage, Traumatic/	231
5	exp Cerebral Hemorrhage, Traumatic/ or exp Hematoma, Epidural, Cranial/ or "extradural haemorrhage".mp.	1434
4	exp Hematoma, Subdural/ or "subdural h#em*".mp.	3712
3	exp Intracranial Hemorrhages/ or "intracranial h#em*".mp.	34253
2	exp Cerebral Hemorrhage/ or "intracerebral h#em*".mp.	14418
1	"head injury".mp. or exp Craniocerebral Trauma/	75438

CINHAL plus access through EBSCO 24/11/2016 1983-2016:

Search Terms	Search Options	
S11	((S3 OR S4 OR S5 OR S6) AND (S3 OR S4 OR S5 OR S6 OR S7)) AND (S8 AND S9 AND S10)	View Results (292)
S10	(S3 OR S4 OR S5 OR S6) AND (S3 OR S4 OR S5 OR S6 OR S7)	View Results (6,995)
S9	S1 OR S2	View Results (17,827)
S8	prognosis or outcome	View Results (592,464)
S7	brain contusion OR cerebral contusion	View Results (106)
S6	extradural haematoma OR extradural hematoma OR (epidural hematoma or epidural hemorrhage)	View Results (753)
S5	intracerebral hemorrhage OR intracerebral haemorrhage OR intracerebral bleed	View Results (2,456)
S`4	intracranial hemorrhage OR intracranial haemorrhage OR intracranial hematoma OR intracranial haematoma	View Results (3,176)
S3	subdural hematoma OR subdural hemorrhage OR subdural haematoma OR subdural haemorrhage	View Results (1,246)
S2	traumatic brain injury	View Results (10,081)
S1	head injury	View Results (7,746)

Cochrane CENTRAL:

Search Name: Prognostic systematic Review

Date Run: 24/11/16 11:33:55.251

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

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

Reference	Population	Study Design	Outcome Measures	Prognostic factors assessed	Results	Quality Appraisal
Nishijima et al 2013 Sacromento USA Variability of ICU Use in adult patients with minor traumatic intra-cranial haemorrhages	Multicenter-8 sites Western USA. All Level 1 Trauma registries searched for ICD-9 codes intra-cranial haemorrhage 2005-2010 Inclusion Criteria: • Age ≥ 18 years • Traumatic ICH • Initial ED GCS 15 • ISS less than 16	Retrospective Cohort Study Objective: 1) assess the variability of ICU use in a cohort of patients with minor traumatic intra-cranial haemorrhages across multiple trauma centres. 2)Estimate the proportion of minor traumatic intracranial haemorrhages patients admitted to ICU that do not receive an ICU intervention	Initial ICU admission from ED Proportion of patients receiving crit care intervention defined as: Neurosurgical intervention Mechanical ventilation Vasopressor/ionotropic use Transfusion blood product Invasive monitoring	Age Initial GCS Initial BP LOS hosp ICU stay Procedures as coded in trauma registry AIS	11240 patients coded as bleeds 771 excluded due to missing data 1412 remaining met inclusion criteria. 888/1412 admitted ICU, significant variation between sites 44/1412 (3.1%) had critical care intervention 6/1412 neurosurgical intervention 847/888 patients admitted ICU no crit care intervention Mean/median GCS=15 Mean/median age= 48	**Study Recruitment: Mod risk bias** Dependent on accuracy on recording on trauma registry. Does have some quality assessment of data imputation Note initial GCS 15- lower risk group **Attrition: Low risk** Follow up only during hospital admission **Prognostic factor measurement: Low risk** Doesn't really apply as testing disposition not outcomes **Outcome measures: Low risk** No measure of outcomes after discharge, but study primarily about disposition. Does not report deaths. **Confounding Factors:** States IIS increases ICU admission- will be related to other injuries **Statistical techniques: low risk** N/A **Overall** Only GCS15 patients with low ISS.
Nishijima et al 2015 Sacromento USA Long-term Neurological Outcomes in Adults with	Level1 trauma centre 2008-2013 Inclusion Criteria: • Age ≥ 18 years • Identified ICH ICD9 code trauma registry • Initial ED GCS 15 • Isolated Head Injury based on AIS score	Retrospective Cohort Study Aim compare long-term neurological outcomes in low- risk patients with traumatic intracranial hemorrhage (tICH) admitted to the ICU (intensive care unit) versus patients admitted	Prospective long term outcome measure at 6 months Either GOS-E 8 fully recovered or GOS-E 1-7 not fully recovered	age sex, mechanism of injury initial ED GCS score, initial (SBP) heart rate, respiratory rate, blood alcohol level, AIS score ISS score INR	188 met inclusion criteria 151/188 complete data= cohort 106 admitted ICU (70%) 45 admitted ED (30%) 1/151 patients neurosurgical intervention as inpatient 1/151 patient died as inpatient 78 (52%) GOS-E 8 at 6 months Does present analysis for outcome at 6 months GOSE but no inpatient measures of deterioration.	**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

Traumatic Intracranial Hemorrhage Admitted to ICU versus Floor	• Age<65 • No evidence midline shift CT • Present on TBI data base due to suspected TBI/evidence of ICH	to the floor.		Rotterdam CT score	Adjusted analysis, floor admission versus ICU had an odds ratio of 0.77 (95% CI [0.36-1.64]) for a GOS-E score of 8 at six months. Mean/median GCS=15 Mean/median age= 40	**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. **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-analysis Only GCS15 patients with benign looking CT scans
Schaller et al 2015 Switzerland	Level 1 Trauma centre Bern Switzerland Jan 2006-Dec 2007 Inclusion criteria: • Admission GCS 13-15 • Observed for 24H • Localised intra-cranial 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	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 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

	• Other injuries • Live alone • Live greater the 1H from hospital					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
Levy et al 2011 Colorado USA	Level 1 Trauma centre Denver USA Jan 1998-Dec 2008 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 **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	ED disposition ICU admission Neurosurgery In-hospital mortality Progression of SAH on CT	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 117 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.

						Can use for pooling for outcomes SAH- supports low risk sub-population
Levy et al 2014 USA	Level III rural non-neurosurgical unit in Rocky mountains April 2007-Dec 2012 April 2007 patients with small bleeds selectively not transferred to neurosurgical unit Inclusion criteria: • Admission GCS 13-15 • CT positive intra-cranial injury • Not transferred to neurosurg unit in accordance with non-transfer policy. • CT findings of small SAH • Punctate or minimal contusion • Punctate or minimal intra-	Retrospective cohort Study Aim Investigate outcomes after a novel non-transfer policy for mTBI patients with small ICH introduced in a small rural trauma unit without neurosurgical cover	Length of stay Mortality Neurological deterioration Neurosurgery Re-admission in 90 days of discharge Inter-hospital transfer Need for repeat CT	No comparison to patients that were transferred	76/273 patients not transferred >50% injuries due to skiing/snow boarding 71% patients less then 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**

	cranial bleed • Small SDH, no mass effect 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					**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	Level 1 Trauma centre 2009-2011 (likely subset of patients presented below) 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 intra-cranial haemorrhage without neurosurgical invlolvement	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	**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. **Attrition: 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 age= 30 Percent anticoagulated=0	**Statistical techniques: High risk** Does not outline how matched groups using propensity scoring General points Small numbers. Likely reporting data reported else where.
AbdelFattah et al 2012 USA	Level 1 trauma center Dallas Texas Prospective recruitment 2010-2011 Inclusion criteria: • Adult with ICH (note doesn't explicitly state 2ndary to trauma- but implied) Excluded: • Age<16 • GCS<13 • Undergone planned or immediate neurosurgery • Transferred patients	Prospective Cohort Study Hypothesis: 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.	Outcome measures during hospital admission: Neurologic progression. Medical intervention Neurosurgical intervention Repeat CT imaging- worse CT defined as worse by a blinded radiologist/neurosurgeon giving qualitative measure of bleed.	Comparison between groups: Age Sex Coagulation status Anti-platelets ISS GCS	145 patients met inclusion/exclusion criteria. 92/145 for routine repeat CT 53/145 for CT if deteriorated Selective group more likely aspirin use P=0.02 Routine repeat CT worse Head AIS score (P<0.001) Otherwise groups comparable 5/53 deteriorated and had a repeat CT + 1/53 had repeat scan as started on warfarin 1/145 patients died (due to other injuries) 27/145 radiological deterioration 9/145 patients intubated- states for other injuries Mean/median GCS=14.5 Mean/median age= 41 Percent anticoagulated=6	**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.
Nayak et al 2013 USA	University Hospital Newark New Jersey Level 1 trauma centre 2003-2008 Inclusion criteria:	Retrospective Chart Review Aim: To compare neurologic outcomes of MHI patients with an intra-cranial bleed	Neurosurgical intervention after 24 hours- craniotomy, ventriculostomy, ICP bolt/measurement Death in hospital	Age Sex Mechanism of Injury GCS on arrival ISS HAIS	321/864 patients GCS13-15 with ICB met inclusion criteria 20% excluded because incomplete medical notes/transfers 0/321 neurosurgical intervention-all within 24 hours of admission No deaths	**Study Recruitment: Low risk** Retrospective case note review- depends on information being recorded correctly. **Attrition: Mod risk** 20% excluded because of incomplete notes

	• Aged 18 and over • Blunt trauma • Intra-cranial bleed • Admitted to hospital • GCS13-15 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	with a normal neurological examination managed with and without a repeat CT head scan	Discharge disposition LOS hospital GOS at f/u clinic/ re-attendance if applicable	GCS and 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	**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.
Anandalwar et al 2016 New Jersey USA	University Hospital Newark New Jersey Level 1 trauma centre 2009-20012 Inclusion criteria: • Aged 18 and over • Blunt trauma • Intra-cranial bleed/skull fracture • Admitted to	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.	Age Sex Mechanism of Injury ISS AIS	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 GCS13-15 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**

	hospital • GCS13-15 on arrival to ED • GCS 15 24 hours after attendance to ED • Did not receive a repeat CT head scan Excluded: • History of neurological or psychiatric disorder • Immediate neurosurgery • Previous TBI or neurosurgery • Spinal injury • Coagulopathy • Pregnancy • Transfers • Incomplete notes Patients that did undergo a repeat CT scan despite meeting the rest of inclusion/exclusion criteria formed a comparison group		ED revisits within 1 year for 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	Potential for patients to have re-attended at other EDs and be missed **Prognostic factor measurement: Low risk** No risk model developed Factors abstracted from case notes **Outcome measures: low risk** Re-attendance at other EDs makes re-attendance a potentially biased outcome measure **Confounding Factors: Mod risk** Cohort includes patients with multiple injuries **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.
Ditty et al 2015 Alabama USA	University Alabama Level 1 trauma centre 2003-20013 Inclusion criteria: • 500 consecutive patients present on trauma registry • GCS13-15 • ICD9 diagnosis SAH and/or intra-parenchymal contusion-	Retrospective Cohort Study **Aim** Assess the clinical implications of SAH or intraparenchymal haemorrhage in mTBI	Neurological decline- altered mental state or focal neurological deficit. Inpatient seizure Delayed neurosurgical evacuation as inpatient. 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-platelts) 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. No details about inclusion or completeness of trauma registry. **Attrition: Low Risk** Only inpatient measures

	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.
Pruitt 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	Retrospective cohort study **Aim** Assess if mTBI patients with intra-cranial haemorrhage can be managed to an ED observation unit	Clinical deterioration (defined as decrease in mental status, worsening neurologic exam or death) Neurosurgery during admission. Progression on CT.	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	1185 GCS13-15 with CT detected injuries 814 admitted directly to hospital- poly-trauma, social reasons or as neurosurgeons felt high risk. 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. **Admitted patients** Clinical deterioration 15/814 Worsening CT 27/814 Neurosurgery 33/814 Composite outcome 75/814 **ED obs unit** Clinical deterioration 0/239 Worsening CT 11/239 Neurosurgery 3/239 Composite outcome 14/239 Medical admission 4/239 Trauma/neurosurgery admit 8/239 **Follow up 190/239** Delayed Neurosurgery 0/239	**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: Med 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.

				radiologist reports- type and size of detected injury	Post traumatic seizure 3/239 Concussive symptoms 16/239 **Discharged ED** **Follow up 111/132** Delayed Neurosurgery 1/132 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	**Confounding Factors: Low risk** Included patients with polytauma 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.
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 13-15head 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

	adults only but age range 15-67					**Statistical techniques: N/A** Too poor quality to include
Kreitzer et al 2014 Cincinnati USA	Level trauma center 2001-2010 Identified from cohort of patients undergone 2 CT within the ED within 24 hours Inclusion criteria: • GCS 14-15 and blunt head injury • Presented within 24 hours injury • Intra-cranial bleed first CT defined extradural, sundural, SAH, intra-cerebral and cerebral contusion • 2nd CT within 24 hours 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>1.4 (even if taking warfarin) • Platelets less than 50 • Any non-head injury mandating admission	Retrospective cohort study Standard practice repeat CT at least 6 hours after 1st CT if mTBI with ICH. If CT and patient stable discharge from ED. Aim: Assess outcomes for patients with mTBI and ICH	Death within 30 days Neurosurgical intervention within 2 weeks Return to the Ed within 7 days of discharge	CT head findings Age Race Sex Medical background	323/1011 patients that under-went 2 CT head within 24 hours in ED met the inclusion criteria After second CT 92/323 admitted 25/323 observed in ED and subsequently discharged 206/323 discharged 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. 3 neurosurgical interventions (all admitted) 28/206 discharged patients returned to ED within 1 week. None re-admitted and some planned- removal of sutures. Mean/median age= 42 Percent anticoagulated=0	**Study Recruitment: Mod risk** 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 **Attrition:Low Risk** Followed up through social security system for deaths and the rest are inpatient outcome. Possibility of patients re-attending at other ED **Prognostic factor measurement: Medium** risk 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 **Outcome measures: low risk** Reasonable outcome measures **Confounding Factors: Low risk** Controls for comorbidities and other injuries **Statistical techniques: N/A**

	• Age less than 18					
Ding et al 2012 Neurosurgical Center China	Neurosurgical Centre China 2009-2010 Inclusion criteria: • All patients with TBI with evidence of intra-cranial haemorrhage- some data for GCS13-15 Excluded: • Immediate neurosurgery • Died within 3 days • Severe multiple injuries • Failed to undergo a repeat CT head	Appears to be a random control trial comparing outcomes in patients with traumatic intra-cranial haemorrhage assigned either to a routine repeat CT or CT only if deteriorates	GCS at discharge Surgical and medical interventions secondary to CT	CT scan results Initial GCS Mechanism of Injury Coagulation INR and platelets	32/89 patients in routine CT group GCS13-15 2/32 worse CT scans No patients had neurosurgery or altered medical management Mean/median age= 48	**Study Recruitment: High risk** Allocation to intervention and non-intervention arm not clearly explained- states via random number generator **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** Controls for other injuries **Statistical techniques: N/A**
Huynh et al 2006 USA	Level 1 trauma centre 2004-2005 Identified case note review 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	Retrospective cohort study **Aim** To assess whether neurosurgical review is necessary in GCS 15 patients with intra-cranial injuries	Changes on follow up CT- all patients had routine repeat CT Neurosurgical intervention	Demographics Mechanism of Injury ISS LOC Amnesia Associated injuries	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 Mean/median GCS=15 Mean/median age= 41	**Study Recruitment: Medium risk** Weaknesses of a retrospective case note review Higher risk group as admitted for at least 48 hours **Attrition: Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** No controls for other injuries

						Statistical techniques: N/A
Almenawer et al 2013 Ontario Canada	Neurosurgical centre Ontario, Canada 2006-2011 Identified from trauma database Inclusion criteria: • GCS13-15 • Blunt traumatic head injury • Age>17 • Intra-cranial injury CT head • Repeat CT scan Excluded: • No repeat CT scan • Previous caniotomy • Cranial pathology • Coagulopathy • Immediate Neurosurgery Patients divided into those underwent intervention due to clinical deterioration or due to repeat CT findings	Retrospective cohort study + meta-analysis to assess whether repeat CT imaging necessary in mTBI with intra-cranial haemorrhage	Intervention including: Mannitol or hypertonic saline Surgical intervention including ICP bolt or craniotomy Neurological changes: decrease GCS, cranial nerve change, vomiting and headache	Demographics GCS ISS	1121 patients with mTBI and ICH 445 met inclusion criteria 91/445 worse CT 21/445 patients neurosurgical 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	**Study Recruitment: High risk** Dependent on accuracy of trauma database Large proportion of mTBI patients with ICH did not meet inclusion criteria- selection out of higher risk patients that did not undergo repeat imaging **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** No control for poly trauma **Statistical techniques: N/A**
Sifri et al 2004 USA	Level Trauma Centre New jersey 1999-2001 Inclusion criteria: • GCS 14-15 • Blunt traumatic head injury • Age>15 • Intra-cranial injury CT head • Repeat CT Excluded:	Retrospective Cohort Study: To assess the value of routine repeat CT imaging in mTBI patients with intra-cranial haemorrhage	Worse CT Inpatient neurological deterioration- abnormal neurology- confusion, disorientation or drowsiness Inpatient neurosurgical interventions	CT results as abstracted from radiologist and neurosurgeons reports. Best ED GCS Demographics	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	**Study Recruitment: Medium risk** Selection out of patients not undergoing repeat CT hea dimaging **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk The definition of abnormal neurology is loose and not clear when it developed- not an admission criteria factor

	• History of brain injury • Coagulopathy including known bleeding disorder or taking warfarin • Immediate neurosurgical intervention including transfer to ICU				50/202 worse CT 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	**Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** No control for poly-trauma and comorbidites **Statistical techniques: N/A**
Phelan et al 2014 Dallas USA	Level 1 Trauma Centre Dallas Texas 2010-2012 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 Excluded: • Ages less than 18 • Pregnant • Prisoners	Retrospective Cohort Study Assess whether outcomes for mTBI with isolated traumatic subarachnoid differ for other kinds of intra-cranial bleeds	Worse repeat CT imaging if any Death Craniotomy	CT findings as reread by a study team member Age ISS HAS Emergency department GCS	77 patients GCS13-15 and traumatic SAH 27/77 scheduled repeat CT 3/27 worse CT 50/77-no routine repeat CT 4/50- unscheduled repeat CT 1/50- clinical deterioration and worse CT 4/77 worse CT 0 neurosurgical intervention	**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 comorbidites **Statistical techniques: N/A**
Homnick et al 2012 New Jersey USA	New Jersey Medical School Level 1 trauma centre 2002-2005 Inclusion criteria: • Age>17 • GCS>12 • TBI with positive initial CT-intracerebral	Retrospective Cohort Study Establish how long intra-cranial bleeds in mTBI continue to expand	Neurosurgical intervention Progression on CT-repeat CTs as discretion of neurosurgeon	Age Sec Pre-injury anti-coagulation Mechanism ISS Initial GCS	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 Mean/median GCS=14.6 Mean/median age= 47	**Study Recruitment: Medium risk** Selection out of lower risk patients that did not have repeat CT imaging **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: low** risk Does not really assess prognostic value of factors measured

	bleed, contusion, subdural, extra-dural or SAH Excluded: • Penetrating trauma • Injury >24 hours previously • Previous neurosurgery • Non-traumatic mass on CT • Immediate neurosurgery				Percent anticoagulated=2	**Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Medium risk** No control for poly-trauma and comorbidites **Statistical techniques: N/A**
Nasir et al 2011 Karachi Pakistan	Specialist Centre Karachi Non-probability consecutive sampling Inclusion criteria: • GCS14-15 • All ages-15% sample children mean age 36 2 SD 18 • TBI with positive initial CT intra-cranial 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 intra-cranial 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	**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 comorbidites **Statistical techniques: N/A** **Overall** Includes kids and quite a different population than North America and Europe.
Boris et 2013 Israel	Israel Level 2 trauma centre Sates 2007-2011 Inclusion criteria:	Retrospective Cohort Study Assess whether repeat CT imaging in GCS14-15 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

	• 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	with intracranial injury justified	New motor or sensory symptoms Severe headache or vomiting		12/68 mild deterioration 28 patients intra-parenchymal bleed 1/28 worse CT 3/28 neurological deterioration 1/28 transferred to neurosurgery (not patient with worse CT) 7 patients extra-dural 1/7 worse CT 0/7 neurological change 1/7 transferred to neurosurgery 20 patients sub-durals 3/20 worse CT 4/20 neurological deterioration 1/20 neurosurgery 13 patietns SAH 3/13 increase in size bleed 5/13 neurological deterioration 1/13 transferred to neurosurgery Mean/median GCS=14.8 Mean/median age= 56	immediately. Likely to be lower risk smaple 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 comorbidites **Statistical techniques: N/A**
Brown et al 2007 Los Angeles USA	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	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	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**

	(mean age 44 +/- 19)					
Thomas et al 2010 Tennesse USA	Tennesse Level 1 trauma centre 50 months from Jan 2001 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 indications • Died before second CT All patients repeat CT at 6-8 hours after admission	Retrospective Cohort Study To assess whether scheduled repeat CT head imaging is indicated in TBI	Neurosurgical interventions- craniotomy or ICP monitor Medical interventions- mannitol/hypertonic saline Neurological change-reduced GCS, pupillary change, increased ICP or loss of brain stem reflexes	Initial GCS ISS Race Age Gender Mechanism of injury History of vascular disease Anticoagulant use Antiplatelet use PT, aPPT, INR CT findings	457/836 in included sample population GCS13-15 14/457= neurosurgical intervention (craniotomy or ICP bolt) 3/457 medical management 5/14 neurosurgical interventions- based on repeat CT 3/14 medical interventions based on repeat CT Mean/median age= 42	**Study Recruitment: Mod risk** Dependent on case note review. Patient with "unclear" indications for interventions removed. **Attrition: Low Risk** Only inpatient outcome measures **Prognostic factor measurement: Mod risk** Does not explain how CT scans reported **Outcome measures: Mod risk** No F/U after discharge **Confounding Factors: Medium risk** No control for poly-trauma **Statistical techniques: N/A** None done
Klein et al 2010 Israel	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 bleed. One hospital transferred all patients to neurosurgical centre. Other 2 hospitals transferred selected	Retrospective Cohort Study **Aim:** Assess the outcome of low risk patients with ICB managed in district hospitals without neurosurgical services	Mortality Neurosurgical intervention Neurological status at discharge	Age AIS ISS	323 patients all 3 hospital intra-cranial bleed and GCS13-15 27/323 required neuro-rehab 2/323 died 35/323 neurosurgery 77/323 not transferred- 0/77 died 0/77 neurosurgery 2/77 delayed transfer Non-transfer on basis of: Single bleed </= 5mm or contusion <1cm and no-coagulopathy Mean/median age= 39	**Study Recruitment: Low risk** Dependent on completeness of trauma registry **Attrition: Low Risk** Only inpatient outcome measures **Prognostic factor measurement: Mod risk** Does not explain how CT scans reported **Outcome measures: Mod risk** No F/U after discharge **Confounding Factors: Medium risk** No control for poly-trauma or comorbidities

	patients.					**Statistical techniques: N/A** None done
Sifri et al 2011 USA	Level 1 Trauma Centre New jersey 2002-2006 Inclusion criteria: • Initial GCS 13-15 • Blunt traumatic head injury • Age 18+ • Intra-cranial injury CT head-ICB or skull fracture • Repeat CT • Abnormal neurological examination at time of repeat CT Excluded: • Immediate or planned neurosurgical intervention • Normal neurology at time of repeat CT- normal neurology defined as GCS15, orientation to place, person or time, normal neurological exam, no symptoms from head injury- headache, vomiting, dizziness, lethargy • Coagulopathy including known bleeding disorder or taking warfarin	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 GOSE at discharge	Demographics Acute deterioration in neurological Exam Persistently Abnormal Neurological exam Unknown whether change as intubated	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	**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

	• Pregnancy • Spinal Cord Injury • Prior Neurosurgical					

Supplementary Material 2: Data Extracted from Included Studies

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

Reference	Population	Study Design	Outcome Measures	Prognostic factors assessed	Results	Quality Appraisal
Nishijima et al 2013 Sacramento USA	Multicenter 8 sites Western USA. All Level 1	Retrospective Cohort Study	Initial ICU admission from ED Proportion of patients receiving crit care intervention defined as: Neurosurgical intervention Mechanical ventilation Vasopressor/ionotropic use Transfusion blood product	Age Initial GCS Initial BP LOS hosp ICU stay Procedures, as coded in trauma registry AIS gender, trauma mechanism, comorbidities, CT findings, repeated CT imaging, age, GCS scores, laboratory values	11240 patients coded as bleeds 771 excluded due to missing data 70 patients met inclusion criteria. 37 no anticoagulation 33 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: Mod risk bias** Dependent on accuracy on recording on trauma registry. Does have some quality assessment of data imputation Although high rates of anti-coagulation. Note initial GCS 15- lower risk group **Attrition: Low Risk** Only inpatient outcome measures Follow up only during hospital admission **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
Bennon et al 2015 Germany	Heidelberg University Hospital, Germany 2013-2014 Inclusion criteria: • Initial GCS 13-15 • Traumatic Intra-cranial bleed CT head	Retrospective Cohort Study **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.	1412 remaining met inclusion criteria. 888/1412 admitted ICU, significant variation between sites 44/1412 (3.1%) had critical care intervention 6/1412 neurosurgical intervention	**Study Recruitment: Low risk** **Attrition: Low risk**
Variability of ICU Use in adult patients	Trauma Registries searched for ICD-9 codes intra-cranial haemorrhage 2005-2010	Objective: 1) assess the variability of ICU use in a cohort of patients with minor traumatic intra-cranial haemorrhages across				

with minor traumatic intra-cranial haemorrhages	• Age ≥ 18 years • Traumatic ICH • Initial ED GCS 15 • ISS less than 16	multiple trauma centres. 2)Estimate the proportion of minor traumatic intracranial haemorrhages patients admitted to ICU that do not receive an ICU intervention	Invasive monitoring		847/888 patients admitted ICU no crit care intervention Mean/median GCS=15 Mean/median age= 48	**Prognostic factor measurement: Low risk** Doesn't really apply as testing disposition not outcomes **Outcome measures: Low risk** No measure of outcomes after discharge, but study primarily about disposition. Does not report deaths. **Confounding Factors:** States IIS increases ICU admission- will be related to other injuries **Statistical techniques: low risk** N/A **Overall** Only GCS15 patients with low ISS.
Nishijima et al 2015 Sacromento USA Long-term Neurological Outcomes in Adults with Traumatic Intracranial Hemorrhage Admitted to ICU versus Floor	Level1 trauma centre 2008-2013 Inclusion Criteria: • Age ≥ 18 years • Identified ICH ICD9 code trauma registry • Initial ED GCS 15 • Isolated Head Injury based on AIS score • Age<65 • No evidence midline shift CT • Present on TBI data base due to suspected TBI/evidence of ICH	Retrospective Cohort Study Aim compare long-term neurological outcomes in low- risk patients with traumatic intracranial hemorrhage (tICH) admitted to the ICU (intensive care unit) versus patients admitted to the floor.	Prospective long term outcome measure at 6 months Either GOS-E 8 fully recovered or GOS-E 1-7 not fully recovered	age sex, mechanism of injury initial ED GCS score, initial (SBP) heart rate, respiratory rate, blood alcohol level, AIS score ISS score INR Rotterdam CT score	188 met inclusion criteria 151/188 complete data= cohort 106 admitted ICU (70%) 45 admitted ED (30%) 1/151 patients neurosurgical intervention as inpatient 1/151 patient died as inpatient 78 (52%) GOS-E 8 at 6 months Does present analysis for outcome at 6 months GOSE but no inpatient measures of deterioration. Adjusted analysis, floor admission versus ICU had an odds ratio of 0.77 (95% CI [0.36-1.64]) for a GOS-E score of 8 at six months. Mean/median GCS=15 Mean/median age= 40	**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** 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. **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-

						analysis Only GCS15 patients with benign looking CT scans
Schaller et al 2015 Switzerland	Level 1 Trauma centre Bern Switzerland Jan 2006-Dec 2007 Inclusion criteria: • Admission GCS 13-15 • Observed for 24H • Localised intra-cranial 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 the 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 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

Levy et al 2011 Colorado USA	Level 1 Trauma centre Denver USA Jan 1998-Dec 2008 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 **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	ED disposition ICU admission Neurosurgery In-hospital mortality Progression of SAH on CT	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 117 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. Can use for pooling for outcomes SAH- supports low risk sub-population

Levy et al 2014 USA	Level III rural non-neurosurgical unit in Rocky mountains April 2007-Dec 2012 April 2007 patients with small bleeds selectively not transferred to neurosurgical unit Inclusion criteria: • Admission GCS 13-15 • CT positive intra-cranial injury • Not transferred to neurosurg unit in accordance with non-transfer policy. • CT findings of small SAH • Punctate or minimal contusion • Punctate or minimal intra-cranial bleed • Small SDH, no mass effect 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	Retrospective cohort Study Aim Investigate outcomes after a novel non-transfer policy for mTBI patients with small ICH introduced in a small rural trauma unit without neurosurgical cover	Length of stay Mortality Neurological deterioration Neurosurgery Re-admission in 90 days of discharge Inter-hospital transfer Need for repeat CT	No comparison to patients that were transferred	76/273 patients not transferred >50% injuries due to skiing/snow boarding 71% patients less then 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 2013 USA The acute care surgery model: Managing traumatic brain injury without an inpatient neurosurgical consultation	Level 1 Trauma centre 2009-2011 (likely subset of patients presented below) 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 intra-cranial haemorrhage without neurosurgical invlolvement	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. **Attrition: 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

					Percent anticoagulated=0	**Statistical techniques: High risk** Does not outline how matched groups using propensity scoring General points Small numbers. Likely reporting data reported else where.
AbdelFattah et al 2012 USA	Level 1 trauma center Dallas Texas Prospective recruitment 2010-2011 Inclusion criteria: • Adult with ICH (note doesn't explicitly state 2ndary to trauma- but implied) Excluded: • Age<16 • GCS<13 • Undergone planned or immediate neurosurgery • Transferred patients	Prospective Cohort Study Hypothesis: 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.	Outcome measures during hospital admission: Neurologic progression. Medical intervention Neurosurgical intervention Repeat CT imaging- worse CT defined as worse by a blinded radiologist/neurosurgeon giving qualitative measure of bleed.	Comparison between groups: Age Sex Coagulation status Anti-platelets ISS GCS	145 patients met inclusion/exclusion criteria. 92/145 for routine repeat CT 53/145 for CT if deteriorated Selective group more likely aspirin use P=0.02 Routine repeat CT worse Head AIS score (P<0.001) Otherwise groups comparable 5/53 deteriorated and had a repeat CT + 1/53 had repeat scan as started on warfarin 1/145 patients died (due to other injuries) 27/145 radiological deterioration 9/145 patients intubated- states for other injuries Mean/median GCS=14.5 Mean/median age= 41 Percent anticoagulated=6	**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.
Nayak et al 2013 USA	University Hospital Newark New Jersey Level 1 trauma centre 2003-2008 Inclusion criteria: • Aged 18 and over	Retrospective Chart Review Aim: To compare neurologic outcomes of MHI patients with an intra-cranial bleed with a normal	Neurosurgical intervention after 24 hours- craniotomy, ventriculostomy, ICP bolt/measurement Death in hospital Discharge disposition	Age Sex Mechanism of Injury GCS on arrival ISS HAIS GCS and	321/864 patients GCS13-15 with ICB met inclusion criteria 20% excluded because incomplete medical notes/transfers 0/321 neurosurgical intervention-all within 24 hours of admission No deaths	**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: Mow risk**

	• Blunt trauma • Intra-cranial bleed • Admitted to hospital • GCS13-15 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	neurological examination managed with and without a repeat CT head scan	LOS hospital GOS at f/u clinic/ re-attendance if applicable	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	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.
Anandalwar et al 2016 New Jersey USA	University Hospital Newark New Jersey Level 1 trauma centre 2009-20012 Inclusion criteria: • Aged 18 and over • Blunt trauma • Intra-cranial bleed/skull fracture • Admitted to hospital	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	Age Sex Mechanism of Injury ISS AIS	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 GCS13-15 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

	• GCS13-15 on arrival to ED • GCS 15 24 hours after attendance to ED • Did not receive a repeat CT head scan Excluded: • History of neurological or psychiatric disorder • Immediate neurosurgery • Previous TBI or neurosurgery • Spinal injury • Coagulopathy • Pregnancy • Transfers • Incomplete notes 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	at other EDs and be missed **Prognostic factor measurement: Low risk** No risk model developed Factors abstracted from case notes **Outcome measures: low risk** Re-attendance at other EDs makes re-attendance a potentially biased outcome measure **Confounding Factors: Mod risk** Cohort includes patients with multiple injuries **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.
Ditty et al 2015 Alabama USA	University Alabama Level 1 trauma centre 2003-20013 Inclusion criteria: • 500 consecutive patients present on trauma registry • GCS13-15 • ICD9 diagnosis SAH and/or intra-parenchymal contusion- confirmed with	Retrospective Cohort Study **Aim** Assess the clinical implications of SAH or intraparenchymal haemorrhage in mTBI	Neurological decline- altered mental state or focal neurological deficit. Inpatient seizure Delayed neurosurgical evacuation as inpatient. 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-platelts) 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. No details about inclusion or completeness of trauma registry. **Attrition: Low Risk** Only inpatient measures

	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.
Pruitt 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	Retrospective cohort study **Aim** Assess if mTBI patients with intra-cranial haemorrhage can be managed to an ED observation unit	Clinical deterioration (defined as decrease in mental status, worsening neurologic exam or death) Neurosurgery during admission. Progression on CT.	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	1185 GCS13-15 with CT detected injuries 814 admitted directly to hospital- poly-trauma, social reasons or as neurosurgeons felt high risk. 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. **Admitted patients** Clinical deterioration 15/814 Worsening CT 27/814 Neurosurgery 33/814 Composite outcome 75/814 **ED obs unit** Clinical deterioration0/239 Worsening CT11/239 Neurosurgery 3/239 Composite outcome 14/239 Medical admission 4/239 Trauma/neurosurgery admit 8/239 **Follow up 190/239** Delayed Neurosurgery0/239 Post traumatic seizure 3/239	**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: Med 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**

				reports- type and size of detected injury	Concussive symptoms 16/239 **Discharged ED** **Follow up 111/132** Delayed Neurosurgery1/132 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 polytauma 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.
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 13-15head 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 **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 **Statistical techniques: N/A**

	range 15-67					Too poor quality to include
Kreitzer et al 2014 Cincinnati USA	Level trauma center 2001-2010 Identified from cohort of patients undergone 2 CT within the ED within 24 hours Inclusion criteria: • GCS 14-15 and blunt head injury • Presented within 24 hours injury • Intra-cranial bleed first CT defined extradural, sundural, SAH, intra-cerebral and cerebral contusion • 2nd CT within 24 hours 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>1.4 (even if taking warfarin) • Platelets less than 50 • Any non-head injury mandating admission • Age less than 18	Retrospective cohort study Standard practice repeat CT at least 6 hours after 1st CT if mTBI with ICH. If CT and patient stable discharge from ED. Aim: Assess outcomes for patients with mTBI and ICH	Death within 30 days Neurosurgical intervention within 2 weeks Return to the Ed within 7 days of discharge	CT head findings Age Race Sex Medical background	323/1011 patients that under-went 2 CT head within 24 hours in ED met the inclusion criteria After second CT 92/323 admitted 25/323 observed in ED and subsequently discharged 206/323 discharged 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. 3 neurosurgical interventions (all admitted) 28/206 discharged patients returned to ED within 1 week. None re-admitted and some planned- removal of sutures. Mean/median age= 42 Percent anticoagulated=0	**Study Recruitment: Mod risk** 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 **Attrition:Low Risk** Followed up through social security system for deaths and the rest are inpatient outcome. Possibility of patients re-attending at other ED **Prognostic factor measurement: Medium risk** 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 **Outcome measures: low risk** Reasonable outcome measures **Confounding Factors: Low risk** Controls for comorbidities and other injuries **Statistical techniques: N/A**

Ding et al 2012 Neurosurgical Center China	Neurosurgical Centre China 2009-2010 Inclusion criteria: • All patients with TBI with evidence of intra-cranial haemorrhage- some data for GCS13-15 Excluded: • Immediate neurosurgery • Died within 3 days • Severe multiple injuries • Failed to undergo a repeat CT head	Appears to be a random control trial comparing outcomes in patients with traumatic intra-cranial haemorrhage assigned either to a routine repeat CT or CT only if deteriorates	GCS at discharge Surgical and medical interventions secondary to CT	CT scan results Initial GCS Mechanism of Injury Coagulation INR and platelets	32/89 patients in routine CT group GCS13-15 2/32 worse CT scans No patients had neurosurgery or altered medical management Mean/median age= 48	**Study Recruitment: High risk** Allocation to intervention and non-intervention arm not clearly explained- states via random number generator **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** Controls for other injuries **Statistical techniques: N/A**
Huynh et al 2006 USA	Level 1 trauma centre 2004-2005 Identified case note review 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	Retrospective cohort study **Aim** To assess whether neurosurgical review is necessary in GCS 15 patients with intra-cranial injuries	Changes on follow up CT- all patients had routine repeat CT Neurosurgical intervention	Demographics Mechanism of Injury ISS LOC Amnesia Associated injuries	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 Mean/median GCS=15 Mean/median age= 41	**Study Recruitment: Medium risk** Weaknesses of a retrospective case note review Higher risk group as admitted for at least 48 hours **Attrition: Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** No controls for other injuries **Statistical techniques: N/A**

Almenawer et al 2013 Ontario Canada	Neurosurgical centre Ontario, Canada 2006-2011 Identified from trauma database Inclusion criteria: • GCS13-15 • Blunt traumatic head injury • Age>17 • Intra-cranial injury CT head • Repeat CT scan Excluded: • No repeat CT scan • Previous caniotomy • Cranial pathology • Coagulopathy • Immediate Neurosurgery Patients divided into those underwent intervention due to clinical deterioration or due to repeat CT findings	Retrospective cohort study + meta-analysis to assess whether repeat CT imaging necessary in mTBI with intra-cranial haemorrhage	Intervention including: Mannitol or hypertonic saline Surgical intervention including ICP bolt or craniotomy Neurological changes: decrease GCS, cranial nerve change, vomiting and headache	Demographics GCS ISS	1121 patients with mTBI and ICH 445 met inclusion criteria 91/445 worse CT 21/445 patients neurosurgical 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	**Study Recruitment: High risk** Dependent on accuracy of trauma database Large proportion of mTBI patients with ICH did not meet inclusion criteria- selection out of higher risk patients that did not undergo repeat imaging **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Low risk** No control for poly trauma **Statistical techniques: N/A**
Sifri et al 2004 USA	Level Trauma Centre New jersey 1999-2001 Inclusion criteria: • GCS 14-15 • Blunt traumatic head injury • Age>15 • Intra-cranial injury CT head • Repeat CT Excluded: • History of brain injury	Retrospective Cohort Study: To assess the value of routine repeat CT imaging in mTBI patients with intra-cranial haemorrhage	Worse CT Inpatient neurological deterioration- abnormal neurology- confusion, disorientation or drowsiness Inpatient neurosurgical interventions	CT results as abstracted from radiologist and neurosurgeons reports. Best ED GCS Demographics	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 50/202 worse CT	**Study Recruitment: Medium risk** Selection out of patients not undergoing repeat CT hea dimaging **Attrition:Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk The definition of abnormal neurology is loose and not clear when it developed- not an admission criteria factor **Outcome measures: Medium risk** No outcome measures after discharge

	• Coagulopathy including known bleeding disorder or taking warfarin • Immediate neurosurgical intervention including transfer to ICU				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	**Confounding Factors: Low risk** No control for poly-trauma and comorbidites **Statistical techniques: N/A**
Phelan et al 2014 Dallas USA	Level 1 Trauma Centre Dallas Texas 2010-2012 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 Excluded: • Ages less than 18 • Pregnant • Prisoners	Retrospective Cohort Study Assess whether outcomes for mTBI with isolated traumatic subarachnoid differ for other kinds of intra-cranial bleeds	Worse repeat CT imaging if any Death Craniotomy	CT findings as reread by a study team member Age ISS HAS Emergency department GCS	77 patients GCS13-15 and traumatic SAH 27/77 scheduled repeat CT 3/27 worse CT 50/77-no routine repeat CT 4/50- unscheduled repeat CT 1/50- clinical deterioration and worse CT 4/77 worse CT 0 neurosurgical intervention	**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 comorbidites **Statistical techniques: N/A**
Homnick et al 2012 New Jersey USA	New Jersey Medical School Level 1 trauma centre 2002-2005 Inclusion criteria: • Age>17 • GCS>12 • TBI with positive initial CT- intracerebral bleed, contusion, subdural, extra-	Retrospective Cohort Study Establish how long intra-cranial bleeds in mTBI continue to expand	Neurosurgical intervention Progression on CT-repeat CTs as discretion of neurosurgeon	Age Sec Pre-injury anti-coagulation Mechanism ISS Initial GCS	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 Mean/median GCS=14.6 Mean/median age= 47 Percent anticoagulated=2	**Study Recruitment: Medium risk** Selection out of lower risk patients that did not have repeat CT imaging **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

	dural or SAH Excluded: • Penetrating trauma • Injury >24 hours previously • Previous neurosurgery • Non-traumatic mass on CT • Immediate neurosurgery					**Confounding Factors: Medium risk** No control for poly-trauma and comorbidites **Statistical techniques: N/A**
Nasir et al 2011 Karachi Pakistan	Specialist Centre Karachi Non-probability consecutive sampling Inclusion criteria: • GCS14-15 • All ages-15% sample children mean age 36 2 SD 18 • TBI with positive initial CT intra-cranial 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 intra-cranial 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	**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 comorbidites **Statistical techniques: N/A** **Overall** Includes kids and quite a different population than North America and Europe.
Boris et 2013 Israel	Israel Level 2 trauma centre Sates 2007-2011 Inclusion criteria: • GCS14-15 • TBI with positive	Retrospective Cohort Study Assess whether repeat CT imaging in GCS14-15 mTBI with intracranial injury justified	Increased size of bleed second CT Clinical deterioration-decrease in GCS New motor or sensory symptoms	Age Sex Initial and follow-up GCS CT findings	68 patients 4 patients transferred to neurosurgery (2 routine) 8/68 patients worse CT 12/68 mild deterioration	**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 immediately. Likely to be lower risk smaple than population of interest.

	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		Severe headache or vomiting		28 patients intra-parenchymal bleed 1/28 worse CT 3/28 neurological deterioration 1/28 transferred to neurosurgery (not patient with worse CT) 7 patients extra-dural 1/7 worse CT 0/7 neurological change 1/7 transferred to neurosurgery 20 patients sub-durals 3/20 worse CT 4/20 neurological deterioration 1/20 neurosurgery 13 patietns SAH 3/13 increase in size bleed 5/13 neurological deterioration 1/13 transferred to neurosurgery Mean/median GCS=14.8 Mean/median age= 56	**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 comorbidites **Statistical techniques: N/A**
Brown et al 2007 Los Angeles USA	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	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**

Thomas et al 2010 Tennesse USA	Tennesse Level 1 trauma centre 50 months from Jan 2001 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 indications • Died before second CT All patients repeat CT at 6-8 hours after admission	Retrospective Cohort Study To assess whether scheduled repeat CT head imaging is indicated in TBI	Neurosurgical interventions- craniotomy or ICP monitor Medical interventions- mannitol/hypertonic saline Neurological change-reduced GCS, pupillary change, increased ICP or loss of brain stem reflexes	Initial GCS ISS Race Age Gender Mechanism of injury History of vascular disease Anticoagulant use Antiplatelet use PT, aPPT, INR CT findings	457/836 in included sample population GCS13-15 14/457= neurosurgical intervention (craniotomy or ICP bolt) 3/457 medical management 5/14 neurosurgical interventions- based on repeat CT 3/14 medical interventions based on repeat CT Mean/median age= 42	**Study Recruitment: Mod risk** Dependent on case note review. Patient with "unclear" indications for interventions removed. **Attrition: Low Risk** Only inpatient outcome measures **Prognostic factor measurement: Mod risk** Does not explain how CT scans reported **Outcome measures: Mod risk** No F/U after discharge **Confounding Factors: Medium risk** No control for poly-trauma **Statistical techniques: N/A** None done
Klein et al 2010 Israel	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 bleed. One hospital transferred all patients to neurosurgical centre. Other 2 hospitals transferred selected patients.	Retrospective Cohort Study **Aim:** Assess the outcome of low risk patients with ICB managed in district hospitals without neurosurgical services	Mortality Neurosurgical intervention Neurological status at discharge	Age AIS ISS	323 patients all 3 hospital intra-cranial bleed and GCS13-15 27/323 required neuro-rehab 2/323 died 35/323 neurosurgery 77/323 not transferred- 0/77 died 0/77 neurosurgery 2/77 delayed transfer Non-transfer on basis of: Single bleed </= 5mm or contusion <1cm and no-coagulopathy Mean/median age= 39	**Study Recruitment: Low risk** Dependent on completeness of trauma registry **Attrition: Low Risk** Only inpatient outcome measures **Prognostic factor measurement: Mod risk** Does not explain how CT scans reported **Outcome measures: Mod risk** No F/U after discharge **Confounding Factors: Medium risk** No control for poly-trauma or comorbidities **Statistical techniques: N/A**

						None done
Sifri et al 2011 USA	Level 1 Trauma Centre New jersey 2002-2006 Inclusion criteria: • Initial GCS 13-15 • Blunt traumatic head injury • Age 18+ • Intra-cranial injury CT head-ICB or skull fracture • Repeat CT • Abnormal neurological examination at time of repeat CT Excluded: • Immediate or planned neurosurgical intervention • Normal neurology at time of repeat CT- normal neurology defined as GCS15, orientation to place, person or time, normal neurological exam, no symptoms from head injury- headache, vomiting, dizziness, lethargy • Coagulopathy including known bleeding disorder or taking warfarin • Pregnancy • Spinal Cord Injury	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 GOSE at discharge	Demographics Acute deterioration in neurological Exam Persistently Abnormal Neurological exam Unknown whether change as intubated	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	**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

	• Prior brain surgery • Acquired or congenital cerebral pathology or existing neurological or psychiatric disorder					
Beynon et al 2015 Germany	Heidelberg University Hospital Germany 2013-2014 Inclusion criteria: • Initial GCS 13-15 • Traumatic Intra-cranial bleed CT head	Retrospective Cohort Study **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 (also included in pooled estimates outcome prevalence)

Reference	Population	Study Design	Outcome Measures	Prognostic factors assessed	Results	Quality Appraisal
Nishijima et al 2014 Sacramento USA	Single-site: Level 1 trauma centre 2009 – 2013 Inclusion Criteria: • Age ≥ 18 years • Consecutive patients • Initial ED GCS 13-15 • CT +ve ICH-SAH, SDH, EDH, intra-ventricular, intra-parachymal bleed/contusion, diffuse axonal injury Exclusions: • Patients with DNACPR • Patients pre-injury anti-coagulant use	Prospective cohort study **Aim:** Derive a clinical decision instrument for patients with mild ICH low risk requiring critical care intervention. **Statistical Method:** Derived clinical decision instrument with binary recursive partitioning (misclassification cost 20:1). Performance of instrument compared to clinical impression.	critical care invention within 48 hours of arrival ED: • Intubation • Neurosurgery including ICP monitoring/ giving mannitol/hypertonic saline • Transfusion RBC/FFP • Vasopressor /ionotrope use • Cardiac arrest/arrhythmia (HR<40, HR>120) • Interventional angiography	Age ≥ 65years Sex Dangerous mechanism (any non-fall from standing mechanism) Pre-injury antiplatelet use (aspirin or clopidogrel) High risk co-morbidity ED Vital signs GCS <15 at admission BP<90 at any point ED Sats <95% at any point ED Lab results: Platelet count INR Haematocrit Initial CT: Midline shift/absence cisterns Depressed skull fracture Non-isolated head	600 patients 71% male 0.5% died + 6.5% neurosurgery + 8.3% intubated 68% GCS 15 93% admitted ICU 19.3% had crit care intervention 9.2% transfusion 8.3% intubation 6.5% Neurosurgical 4 predictors need for crit care intervention: (Recursive partitioning) GCS<15 (RR 2.95; 95% CI 2.21-4.12) ≥ 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) Sensitivity of decision rule to predict intubation/neurosurgery within 48 hours of admission ED. 98.6% specificity 36.6% To any crit care inteverntion 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%) Clinician 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%) Clinical impression deterioration in 48 hours? Sensitivity 91% 95% C.I. (84.2-95.0%) Specificity 39.5% 95% C.I. (35.1-44.1%) 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)	**Study Recruitment: Mod risk bias** Missed 20% eligible patients- not completely clear individuals in cohort identified. Otherwise clear inclusion and exclusion criteria. **Attrition: Low risk** Follow up only 48 hours so low risk of attrition bias. **Prognostic factor measurement: Low risk** Standardised and objective prognostic factor measurement. Collected all patients. **Outcome measures: Low risk** Recorded in uniform way for all patients. Only 48 hours. **Confounding Factors: Mod Risk** Additional severe injury may be related to prognostic factors and outcome measures. Not accounted for in in analysis. **Statistical techniques: low risk** Good presentation of methods **Overall summary** Risk factors identified by case note review/d/w treating physicans where not clear. Radiology attending written report used for CT findings. No independent quality verification- could introduce bias. CT end point also missed spectrum of possible

				injury AIS score 3 or more additional injury	Hypotension prior to admission RR (95% CI) 2.70 (1.61-4.54) Presence of depressed skull fracture RR (95% CI) 2.44 (1.46-4.08) Presence of any high-risk co-morbidity 1.58 (1.07-2.33) RR (95% CI) Pre-injury antiplatelet use 1.54 (1.04-2.30) RR (95% CI) Hypoxia prior to admission 1.52 (1.03-2.24) Age 65 years or older RR (95% CI) 1.46 (1.05-2.03) Non-fall from standing mechanism of injury RR (95% CI) 1.12 (0.80-1.57) Mean/median GCS=14.6 Mean/median age= 52 Percent anticoagulated=0	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.
Sweeney et al 2015 USA	Identified on national trauma data base 2007-2012 Inclusion criteria: • Age ≥ 18 years • ED inital GCS 14-15 • ICD 9 code intra-cranial injury= cerebral contusion, SAH, SDH, EDH, multiple TBI • Admitted to hospital Exclusions: • ICD9 diagnoses skull fractures • Penetrating mechanism of	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.	ISS (measure of head injury severity due to exclusion criteria). Coagulopathy (pooled measure of Vit K deficiency, haemophilia, thrombocytopaenia, chronic anti-coagulant therapy) Chronic aspirin use not included. Type of intra-cranial injury as per ICD 9 code. ED vital signs Age	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 data base 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 systemically 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

	injury • 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	information. **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 Is MTBI defined by GCS: is it really mild?	Level 1 trauma center Arizona Retrospective case note review 2009-2012 Inclusion criteria: • Initial GCS13-15 • Aged 18+ • Initial scan +VE ICH/skull fracture and routine repeat	Retrospective Chart Review **Aim** Identify factors that predict progression on CT imaging and neurosurgical intervention in GCS13-15 patients . **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 fractue 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-coagulatants and anti-platelts **Attrition: low risk** Outcomes only as inpatients **Prognostic factor measurement: Low risk** Relies on accuracy of medical notes. Re-examines CT images

	scan 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.	imaging within 6 hours of initial CT imaging. Univariate analysis to identify risk factors for progression on CT or neurosurgery. P=/<0.2 included multivariate analysis		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 OR2.6 (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 OR1.1 (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 P=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 OR1.8 (0.9-3.4) BP<90 p=0.35 OR 1.3 (0.45-1.9) Mechanism P=0.34 OR1.2 (0.4-1.8) LOC p=0.19 OR1.4 (0.7-3.2) HR>100 P=0.26 OR 1.5 (0.9-2.8) Displaced skull fractue P=0.01 OR 16 (7.6-19.6) SDH >10mm p=0.001 OR3.9 (2.4-5.1) EDH >10mm p=0.03 OR4.8 (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 OR3.6 (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 OR1.2 (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 P=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 OR1.9 (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.**

					Mean/median age= 54 Percent anticoagulated=0	
Borczuk et al 2013 USA	Level 1 trauma centre Boston Case note review 2009-2010 patients identified through ED electronic coding ICD9 coding for intra-cranial haemorrhage. Inclusion criteria • GCS 13-15 • Age 15 or older • CT positive traumatic intra-cranial haemorrhage Excluded: • Isolated Skull fractures	Described as a cross sectional study 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 **Method** Univariate analysis to predict composite outcome of deterioration 3 factor multivariate model derived from univariate analysis	Deterioration whilst in hospital including: Decrease in GCS Worsening neurological examination Worsening CT result on repeat CT Neurosurgery Death Composite outcome All outcomes whilst in hospital- no discharge outcomes	Data extracted from case notes by 2 ED researchers. Not blinded to the hypothesis Age Method of arrival History of HTN Anti-coagulation Mechanism Initial GCS Neurological examination Alcohol Intoxication Initial platelet count INR Initial CT result F/U CT result CT categorised by attending radiologist type, location and size of bleed/contusion. Presence of midline shift	404/863 TBI patients met inclusion criteria (46.8% patients with traumatic bleeds). 11.8%(48) deteriorated 5.9% neurosurgical Deterioration stratified by injury: 24/136 isolated SDH 0/1 isolated EDH 1/75 isolated SAH 2/31 contusions 22/161 mixed lesions Univariate predictors of deterioration: Age 65+ OR 0.93 95%CI 0.5-1.69 Sex OR 0.77 95%CI 0.41-1.41 Fall OR 0.57 95%CI 0.29-1.09 Assault OR 1.07 95% CI 0.45-2.51 RTC OR 0.51 95%CI 0.12-2.21 Pedestrian Struck OR1.12 95% CI0.32-3.92 Bicycle Struck OR 1.51 95%CI 0.42-5.44 HTN OR0.94 95%C.I. 0.51-1.73 Aspirin OR 0.79 95% CI0.41-1.51 Warfarin OR0.87 95% CI 0.33-2.32 Clopidogrel OR1.25 95% CI 0.27-5.75 GCS<15 OR 2.12 95% CI 1.01-4.43 CT findings Any lesions SDH OR 2.64 95% CI 1.20-5.83 EDH OR 2.4 95% CI 0.91-6.31 SAH OR 0.42 95% CI 0.22-0.81 Contusion OR 0.79 95% 0.39-1.62 Isolated lesions SDH OR 1.62 95% CI 0.88-2.96 EDH OR only 1 patient SAH OR 0.078 95% CI 0.01-0.59 Contusion OR 0.46 95% 0.11-1.96 Multiple logistic regression with 3 variables GCS=15, presence SDH and presence isolated SAH: All remained significant predictors of deterioration. Sensitivity 97.9% and specificity 20.8%	**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

					Negative predictive value 99.6% Positive predictive value 38.8% Mean/median GCS=14.8 Mean/median age= 60 Percent anticoagulated=10	
Washington et al 2012 USA	Level I trauma center Washington Retrospective case note 2-year period (January 2007-December 2008) Inclusion criteria: • Admission GCS score ≥ 13 • Isolated head injury with no other injury requiring ICU admission • Initial head CT scan positive for any type of ICH • Initial non-operative. management plan Excluded: • Patients requiring immediate neurosurgery surgery	Retrospective Cohort Study **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 an 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% C.I.(2.20–14.89) age ≥65 yrs OR4.00 C.I>(1.40–11.42) antiplatelet &/or Coumadin therapy OR 2.94 C.I. (1.12–7.71) Unclear which other factors assessed. States: “multivariate analysis was performed, only an ICH volume > 10 ml was	**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 Death Neurosurgical intervention Worse CT if performed- worsening in Marshall criteria or significant expansion in volume- neuroradiologist GOS outcome at 6 months	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) 7/757deaths 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<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

						presented only as P values. Performed multivariate stepwise regression- for mortality reports 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.
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	Retrospective chart review **Aim:** To determine risk factors with delayed subdural enlargement leading to surgery in patients with acute subdurals	Delayed surgical evacuation of subdural haematoma	Age Gender Cause of trauma Presence of other CT findings GCS Neurological deficit Comorbidities History of antiplatelets Anticoagulation therapy INR Platelet count	98 patients included 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 antiplatelet 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

	15 • Other significant injuries • Patients refusing surgery				Presence of SAH, P=0.003* Diffuse cortical atrophy Mean bifrontal ratio (range)P= 0.345 Mean Sylvian fissure ratio (range) P=0.602 Multivariate analysis of prediction of delayed haematoma evacuation. Maximal thickness P=0.527 OR 2.5 (0.5-41.1) Volume haematoma P=0.01 OR= 1.1 (1.02 -1.17) Midline shift P=0.01 OR=1.43 (1.09-1.89) Cerebral contusion P=0.92 OR 0.85 (0.18-3.97) SAH P=0.43 OR 0.53 (0.11-2.56)	studies. The neurosurgical rate for these injuries appears v. high ?length of follow up. These patients have been discharged and then undergone reimaging as outpatients. Doesn't preclude early discharge of some of these patients but they will need to be followed up.
Overton et al 2014 USA Can trauma surgeons manage mild traumatic brain injuries? Journal: American Journal of Surgery	Level 1 Trauma centre 2006-2012 Inclusion criteria: • Intra-cranial bleed less than 1 cm • to hospital • GCS13-15 on arrival to ED Excluded: • Multiple injuries on CT • Transferred to other care facility • Left against advice Doesn't state only adults but results presented only for adults.	Retrospective Cohort Study **Aim** Reports initial experience with the management of MTBI by trauma surgeons alone. Hypothesize that patients with MTBI managed by trauma surgeons will be the same as outcomes for patients managed by neurosurgeons.	Outcome measured GOS score at discharge 1= death 2=severe disability 3=mod disability 4= full recovery **Method** Mulitvariate regression analysis to assess whether admission under trauma surgeons affected likelihood of GOS >3 (good recovery)	trauma versus neurosurgical management age, sex, race/ethnicity, injury severity, insurance status GCS	171 patients 8 deaths 4 severe disability 24 moderate disability Neurosurgeons managed 120 Trauma surgeon 51 Multivariate regression analysis to predict GOS >3 (full recovery) Admission Trauma surgeon P=0.3OR 1.74(0.61–4.92) Age P<0.001OR0.94 (0.91–0.96) ISS P<0.001 OR0.87 (0.81–0.94) GCS P=0.005 OR13.96(2.23–87.3) Other factors in model but no results reported: sex, ethnicity, ISS, insurance status 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,

						race, ISS, insurance status and GCS motor scores- presents the analysis for only some of these. **Overall** Limited by inclusion criteria of less than 1cm and even though no difference in outcomes with who patients were admitted under, potentially the patient groups received different care.
Schwed et al 2016 California USA	UCLA California Level 1 trauma centre 2012-2015 Inclusion criteria: • Patients identified on trauma registry and case note review • Initial GCS13-15 • 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	Retrospective cohort study **Aim** Identify admission variables associated with favourable outcomes with mTBI and intra-cranial haemorrhage **Method** Univariate and multi-variate regression analysis prediction of "favourable outcome composite measure"	**Favorable outcome-** composite outcome 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.	Vital signs AIS ISS CT findings-Marshall and Rotterdam scores	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 GCS15 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 outcomes 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

					SAH P=0.02 Combination P=0.002 All factors statistically significant in univariate analysis were assessed in multivariate analysis Multivariate model predicting favourable outcome: including ED BP, Marshall score, Isolated SAH, Head AIS, ISS<25, GCS15 at ICU admission and age<55 GCS 15 at ICU admission OR 5.5 95% CI (1.6-18.8) P=0.006 Isolated SAH 5.1 95% C.I. (1.5-17.6) P=0.01 Age<55 OR 3.5 95% C.I. (1.1-11.2) P=0.03 Mean/median age= 60	
Thorson et al 2012 Miami USA	Miami Level 1 trauma centre 1996-2010 Inclusion criteria: • Initial GCS13-15 • 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). Note neurosurgeons decided whether a	Retrospective cohort study **Aim** To test whether routine CT imaging in mTBI with detected intra-cranial injuries provides useful information in the absence of neurological deterioration **Methods** Step wise multi-variate regression for factors P<0.2 associated with progression on CT and craniotomy	Progression of initial lesion or new lesion identified. Neurosurgical intervention. Death.	CT findings- including type of injury, presence of oedema, mass effect or herniation. Age Sex ISS GCS Abnormal neurological examination- change in GCS greater than 1, GCS less than 13,Neurological deficit, or significant symptoms including headache, lethargy, visual disturbance.	1510 patients with GCS13-15 and head injury 537/1510 +ve initial CT scans 62 proceeded immediately to surgery and 115 no repeat CT in 24 hours- (mostly as the neurosurgeon deemed injury insignificant). 360/537 had repeat CT imaging. 11% of repeat CT scans-recalled (i.e.no actual injury) 108/360- progression on CT imaging Mean/median GCS=14.5 Mean/median age= 47 Percent anticoagulated=3 Age No change 46 SD 20 Progression 50 D 23 P=0.13 Sex No Change Male 178 Progression 79 P0.11 Intubated No Change 22 Progression 17 P=0.05 ISS No change 12 SD 5 Progression 15 SD 6 P<0.01 GCS 15 arrival No Change 158 Progression 37 GCS 14 No Change 65 Progression 43 GCS 13 No Change 31 Progression 28 Anticoagulant Use No Change 17 progression 11 0.29 Aspirin No Change 7 Progression 3 Plavix No Change 1 Progression 2 Coumadin No change 2 Progression 4 LMWH No Change 2 Progression 0 Multiple No Change 5 Progression 2 PT No Change 12.2 Progression 12.6 P= 0.443 PTT No Change 25.2 Progression 24.8 P=0.85	**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 47 SD 21 Neuro Surg 51 D 23 P=0.97 Sex No Neuro Surg Male 241 Neuro Surg 22 P0.11 ISS No Neuro Surg 13 SD 5 Neuro Surg 17 SD 6 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 OR4 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%C.I. (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 95% 1.64-20) New/worse herniation 32.1 95% C.I. 7.83-131.6 P=0.001	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 USA	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	**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:**

	• Present on trauma registry • Initial GCS13-15 • Isolated subarachnoid haemorrhage • Does not state adult only but mean age 65.7	analysis computed with step-down logistic regression- discharge home primary outcome			1/479 to hospice 6 week follow up 1/478 bilsteral subdural- drained States surgical intervention 0.2% Step down Multivariate regression with outcome discharge home Age P<0.0001 Admission GCS P=0.0018 ISS P=0.0088 Not progression of bleed on CT	**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.
Velmahos et al 2006 Massachusetts USA	Massachusetts Level 1 trauma centre 2003-2004 All patients with intra-cranial injuries identified reviewed by a neurosurgeon and repeat CT scheduled within 24 hours. Inclusion criteria: • Present on trauma registry • Initial GCS13-	Retrospective cohort study Comparison univariate characteristic patients with worse CT scans compared with the same or improved. Where P value 0.2 or less included in stepwise logistic regression model	Surgical or medical intervention following repeat CT (caniotomy, ICP monitoring, intubation or mannitol, increased ventilation, CSF drain, sedation, transfer to ICU) Worse repeat CT	Demographics ISS Admission observations Time interval between admission and 1st CT and subsequent CT scans	692 patients had CT for head injury 179/692- for scheduled repeat CT 154/692 repeat CT due to intracranial injury 25 no lesion- repeat CT due to anti-coagulation 37/154 worse CT 7/154- medical or surgical intervention due to deterioration 4/154 neursourgical 8/179 deaths 1/44 subdurals neurosurg 0/33 SAH neurosurg 1/13 intra-parenchymal neurosurg 0/7 extra-durals 2/57 multiple neurosurgical Male P=0.44 Age (years) P0.01	**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.

	15 • Blunt head injury • Repeat CT for intra-cranial injury • Presumably adults age presented as mean 48 and SD 25				≤65 P<0.01 Mechanism of blunt trauma P= 0.31 Fall Road traffic accident Other 0.31 Injury Severity Score P=0.01 ISS>16 0.09 Glasgow Coma Scale score on arrival P=0.02 Systolic Blood Pressure on arrival (mm Hg) P= 0.63 Anticoagulation therapy P=0.25 Time from arrival to CT P<0.01 First head CT findings solitary or multiple findings P<0.01 Time between first and second CT P=0.10 Stepwise logistic regression model to predict worse CT Time from injury to CT <90 mins OR6.37 95% CI 2.29-17.76 P<0.1 Age>65 OR3.33 95% CI 1.29-8.60 P=0.01 GCS<15 OR 3.13 95% 1.23-8.01 P=0.02 Multiple lesions OR 11.03 95% CI 1.32-92.06 P=0.03 AUC ROC curve 0.83 If all 4 factors present 83% chance worse CT If none present 2% chance worse CT Mean/median GCS=14.7 Mean/median age= 51 Percent anticoagulated=10	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.
Fabbri et al 2013 Italy- multicenter	Multi-centre 32 Italian hospital- both specialist and general 2009 Inclusion criteria: • Any GCS • 18+ • Head abbreviated AIS 1 or greater • No indication for neurosurgery within 7 days	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	Worse repeat CT defined as increase point on Marshal criteria within 24 hours Neurosurgery within 7 days GOS at 6 months	Age Sex Mechanism Coagulation GCS Anti-platelet medications Type of injury on CT Marshal Classification	Study of all GCS patients but present data for GCS14-15: 1123/1558 patients GCS14-15 Antiplatlet therapy increased the risk of a worse CT: When 2 or less lesions RR 1.86 95% CI 1.06-3.30 P=0.032 When 3+lesions RR 3.34 95% CI 1.74-6.40 P=0.003 87/1123 Worse Characteristic on CT Mean/median age= 65	**Study Recruitment: Mod risk** The paper is not clear about how patients were identified and data extracted Also patients requiring emergency surgery within 7 days based on initial CT excluded- may select out higher risk groups- in practice excluded Marshall 5/6 patients which is reasonable **Attrition: Low Risk** No loss to follow up and standard care for all patients to be reviewed at 6 months **Prognostic factor measurement:**

	• Marshal category 2-4 • Within 24 hours of injury Excluded: • Need immediate neurosurgery • GCS 3 fixed dilated pupils • Unclear history of mechanism • Hypotension< 90 systolic • Penetrating Injuries • Discharge against medical advice					**Low risk** Scans all re-reported **Outcome measures: Low risk** Good outcome end points **Confounding Factors: Mod risk** Not isolated head trauma and state no need to control for comorbidities as shown not to affect head injury outcome **Statistical techniques: Low Risk** Appropriate and well presented **General comments:** Good study Fabbri previously shared data- ?request GCS13-15 subset
Shih et al Taiwan 2016	Tertiary referral Teaching hospital Taiwan No time frame given 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 All patients	Retrospective cohort study **Aim** Determine the potential risk factors of delayed neurosurgical intervention in mTBI with intra-cranial 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	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 0.105–2.228 Diabetes mellitus P=1.000 OR 1.028 95% CI 0.221–4.780 (!?)0 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** Only inpatient measures- 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 heamorrhageP=0.149 Multiple intracranial heamorrhage P=0.149 EDH P ≤0.001 OR 9.923 95% CI 3.105–31.708 SDH P=1.000 OR 0.906 95% 0.298–2.753 IPH P=0.366 OR1.812 95% CI 0.594–5.526 SAH P=0.044 OR0.251 95% CI 0.068–929 IVH P= 0.111 OR13.542 95% CI 1.147–159.876 Midline shift P≤0.001 OR19.813 95% CI5.495–71.435 Skull fracture P≤0.001 OR21.750 95% CI4.707–100.510 Pneumocranium P=0.621 Volume of EDH P≤0.001 Volume of SDH P=0.092 Volume of IPH 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	Also some apparent mistakes in univariate analysis **General comments:** Does not report outcomes by single lesion type
Bardes et al 2016 USA	Level 1 trauma centre West Virginia 2009-2011 All mTBI patients with bleeds admitted to general surgical ICU with a neurosurgical consultation Inclusion criteria: • Blunt TBI • Age>18 • GCS13-15	Retrospective Cohort study **Aim:** Identify low risk mTBI patients with intra-cranial bleeds that do not require admission to ICU	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 53/389 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=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

	• ISS<25 Excluded: • Penetrating injury • GCS<13 States in results all patients had evidence of intra-cranial haemorrhage on bleed- doesn't define what this includes				ICB P=0.051 Aspirin P=0.54 Clopidogrel P=0.17 PT P=0.042 aPPT P=0.0028 Admision INR P=0.42 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	**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 Malaysia	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	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). Surgical interventions: craniotomy, intracranial pressure monitor placement or intubation.	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 admissionP0.009 INR on admission P=3 0.388 Stepwise multiple logistic regression model	**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**

	• suspected drug or alcohol intoxication, • Neurological impairment trauma • Immediate neurosurgery • Admitted ICU for close observation				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) 44/144 multiple lesion worse CT Mean/median GCS=14.6 Mean/median age= 39 Percent anticoagulated=0	Possibility of anti-coagulants. Not recorded. **Statistical techniques: Mow risk** Stats do not present what the risk measure is- presumably an OR. Also selective reporting of significant results. Only for progression on CT- dubious value
Sumritpradit et al 2016 Bangkok Thailand	Patients admitted to an Acute Care Unit surgery 2009-2013 Inclusion criteria: • Admission<72 hours • 16 years and older • positive initial head CT • 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	Age Sex Co-morbidities Medications Initial GCS AIS Medications CT findings	145 patients matched inclusion criteria 98/145 GCS13-15 74/98 routine repeated CT scans (36/98 worse) (1/74 neurosurgical) 24/98 clinically deteriorated and underwent CT imaging (7/28 neurosurgery) Overall 8/98 GCS13-15 patients neurosurgery 24/98 some clinical deterioration-prompting repeat CT GCS13-15 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	**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 delt with **Statistical techniques: Low risk**

					Heart rate on admission, mean p= 0.095 Epidural hematoma P= 1.000 Subdural hematoma P=0.136 Subarachnoid haemorrhage P=0.464 Hemorrhagic contusion P=0.715 Intraventricular hemorrhage P=1.000 Diffuse axonal injury P=) 1.000 Skull fracture P=1.000 Base of skull fracture=0.409 Midline shift > 2 mm P=0.003 Duration from injury to 1st CT P=0.603 Odds ratios associated with these factors reported separately: Subdural hematoma OR 5.3 95%CI (0.63–45.33) P=0.136 Hypertension OR 4.1 95% CI (0.78–21.46) P=0.135 AIS > 4 OR 4.0 95%CI (0.91–17.55) P=0.073 Ischemic heart disease OR 4.8 95% C.I. (0.99–23.19) P=0.070 Clopidogrel OR 10.2 95C.I. (1.87–55.38 P=0.017 Midline shift > 2 mm OR11.9 95% C.I. (2.50–57.20) P=0.003 Neurological deterioration resulting in CT OR 30.0 95% C.I. (3.46–280.83) P<0.001 Mean/median age= 57 Percent anticoagulated=4	Presents simple univariate analysis between neurosurgical and non-neurosurgical patients Is a higher risk population due to selection for repeat CT imaging- possibly unable to include in any meta-analysis.
Sifri et al 2006 New Jersey USA	New Jersey Level 1 trauma centre 2002-2003 12 months Inclusion criteria: • Initial GCS13-15 • 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 GCS13-15 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. 0/99 neurosurgery 1/99 death (unrelated to intra-cranial injury) 13% 99 CT scans worse 2/31 neurosurgery 5/31 deaths 14/31 repeat CTs worse Abnormal neurological exam predicts changes repeat CT OR 5.28 CI2.08-13.4 P=0.002 Mean/median GCS=14.6 Mean/median age= 45	**Study Recruitment: Mod risk** Only patients with repeat CT- likely to be a higher risk group **Attrition: Low Risk** Only inpatient measures **Prognostic factor measurement: Mod risk** Does not try and grade severity of CT findings as predictor. Loose definition for abnormal neurology- sometimes prompted repeat CT and no uniformed time when all CT scans performed. **Outcome measures: Mod risk** Only inpatient related outcome measures.

	chronic neurological condition like dementia • Concurrent spinal injury • Anti-coagulated or existing clotting disorder • Patients that underwent immediate or planned neurosurgery due to first CT Patients that only underwent 1 CT				Percent anticoagulated=0	**Confounding Factors: Mod risk** Cohort includes patients with multiple injuries and abnormal observations **Statistical techniques: Low Risk** Minimal statistical analysis
Bee et al 2009 Tennessee USA	Level 1 trauma centre 2005-2007 Identified from trauma registry All patients admitted to ICU under neurosurgeon and received a repeat CT scan Inclusion criteria: • mTBI • Blunt trauma to head • GCS 14-15 • Intra-cranial injury CT head Excluded: • Facial or skull fractures • Immediate neurosurgery • Other injuries requiring ICU	Retrospective cohort study **Aim** Assess whether repeat CT imaging and ICU admission necessary in mTBI with intra-cranial injury	Worse CT Clinical examination change Neurosurgical intervention	Age Sex Admission observations AIS ISS Admission GCS	207 patients met inclusion criteria 58/207 worse CT or neurology requiring intervention (4 neurology only) 31/77 patients multiple/mixed lesions worse CT 18/207 neurosurgery 2 deaths (1 due to stoke other following craniotomy) 5/18 neurosurgical= subdurals with no clinical change but worse CT Univariate Comparison Worsening CT or worsening neurology requiring an intervention versus no deterioration (58 versus 149) Average age worse 47 (47.2 +/-19.8) No worse 45 (45.5+/- 18.7) P=0.56 Average admission SBP worse 152 (152.3 +/-28.3) No worse 143 (143.1+/- 25.9) P=0.03 Average admission pulse worse 87 (86.9 +/-15.3) No worse 88 (88.5+/- 16.1) P=0.556 Average HAIS worse 4.2 (4.21 +/-0.55) No worse 3.8 (3.84+/- 0.54) P<0.0001 Average ISS worse 22.3 (22.3 +/-6.25) No worse 19.6 (19.6+/- 6.9) P=0.018 Mean/median age= 46	**Study Recruitment: low risk** Dependent on accuracy of trauma registry **Attrition: Low Risk** Low risk- inpatient outcomes **Prognostic factor measurement: Medium** risk No re-reporting of CTS **Outcome measures: Medium risk** No outcome measures after discharge **Confounding Factors: Medium risk** No control for comorbidities **Statistical techniques: Low Risk** Higher rates of adverse outcome than other studies

	admission Data only presented for adults (15-94)					
Darby MSc Thesis 2015 USA	Level 1 trauma centre California 2007-2011 Patients identified on a hospital trauma registry Inclusion criteria: • Initial GCS13-15 • Blunt head trauma • Positive CT scan. • 2 or more CT scans • 18+ Excluded: • Pregnant • Age<18 • Penetrating injury	Retrospective Cohort Study: To assess whether GCS 15 patients with intra-cranial haemorrhage that maintain a GCS of 15 benefit from routine CT imaging	Worse repeat CT imaging Neurosurgical outcomes	Age/ Age 65 + Anti-coagulant Medication ISS LOC Skull fracture displaced/undisplaced Neurological symptoms Time interval between scans GCS/deterioration in GCS	658 patients GCS13-15 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) Adjustede 1.1 (0.99-1.05) P=0.27 Age Unadjusted1.01 (95% C.I. 1-10.2) Adjustede 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) ajusted 1.11 (0.96-1.28)	**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.
Fabbri et al 2008 Italian	District general hospital rural Italy Prospective recruitment from	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.	

	1999-2006 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)

Reference	Population	Study Design	Outcome Measures	Prognostic factors assessed	Results	Quality Appraisal
Joseph et al 2014 USA Study 1: defining the BIG criteria	Level 1 Trauma centre 2009-2011 Inclusion criteria: • All TBI patients with CT findings = skull fracture/ ICH 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	Retrospective Cohort Study- 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	Neurosurgical intervention Progression of CT findings on a repeated scan Neurological deterioration if BIG 1 or 2- GCS<12, abnormal focal neurology or abnormal pupils	Anticoagulation Anti-platelets OBS on admission to ED GCS Intoxication CT head scans all reviewed by a single investigator to give size of bleed and associated findings	1232 patients TBI with positive CT scan 121=BIG 1 313=BIG 2 798=BIG 3 888/1232 underwent repeat CT 13% (159) patients neurosurgical outcome- 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% neurosurgical intervention	**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 **Prognostic factor measurement: Mod risk** 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 1 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. Statistically significant reduction in hospital admissions, ICU admissions and repeat CT imaging in prospective cohort post implementation of BIG criteria. 0 30 day readmissions although 5 ED visits	**Study Recruitment: mod risk** States GCS13-15 and range presented as GCS13-15 but also excludes unexaminable patients and patients with altered mental state- appears cohort does not contain all GCS 14 and 13 patients. Not clear about 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.

	neurosurgical intervention • 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.
Joseph et al 2015 USA Study 2:further validation of BIG criteria	Pre BIG TBI March 2011-Feb 2012 Post BIG July 2012-June 2013 Level 1 Trauma centre Inclusion criteria: • All patients with blunt trauma mechanism and ICH/Skull fracture Excluded: • Transfers • Dead on arrival • Needed immediate neurosurgery. Presents subgroup analysis of BIG 1 patients 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	Prospective cohort study Compare outcomes in TBI before and after implementation of BIG criteria	Number of routine repeat CT head scans Neurosurgical consultations Progression of bleed on CT Neurosurgical intervention during hospital admission (craniotomy, craniectomy ICP monitoring) ICU admission 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	Pre BIG 87 BIG 1/415 0 neurosurgery 0 deaths 3 progression on CT 68 (78%)admitted 24 (27.5%) admitted ICU 76 (87.4%) neurosurg consultations 59 (67.8%) repeat CT Post Big 83 BIG 1/381 0 neurosurgery 0 deaths 1 progression on CT 42 admitted (50.6%) 6 ICU admission (7.2%) 7 (8.4%) neurosurg consultation 6 (7.2%) repeat CT Statistically significant (P<0.001 admission hospital, ICU, repeat CT imaging and neurosurgical consultation post introduction of BIG criteria)	**Study Recruitment: Low risk** States all patients with TBI prospectively recorded on data- not cleat how patients identified and recruited. Emergent neurosurgical patients excluded- no definition given **Attrition: low risk** Outcomes only as inpatients or if re-present **Prognostic factor measurement: Mod risk** Ct are reviewed by a member of study group- the cut offs are slightly subjective on CT measurement **Outcome measures: Mod risk** Only measures as inpatient/re-presentation. Potential for discharge and deterioration. **Confounding Factors: low risk** Age **Statistical techniques: Mod risk** Presents data for all patients or BIG 1 patients- not all GCS13-15 patients

	• single IPH					

Supplementary Material 3: Table of Full Studies Retrieved and Excluded

No.	Study	Reason Excluded
1.	Anonymous et al[31] (Full study revealed duplicate of Corrigendum et al[146])	Unable to differentiate initial GCS13-15 patients
2.	Bajsarowicz et al[34]	Abstract only
3.	Bajsarowicz et al[33]	Unable to differentiate initial GCS13-15 patients
4.	Baldawa et al[35]	Letter about included study
5.	Basahm et al[36]	Unable to differentiate initial GCS13-15 patients
6.	Carlson et al[38]	Included paediatric patients and patients with no injuries identified by CT imaging
7.	Chen et al[39]	Uses lumbar puncture to diagnose brain injury
8.	Choudhry et al[41]	Duplicate study[40]
9.	Flaherty et al[43]	Abstract only
10.	Gore et al[44]	Abstract only
11.	Iaccarino et al[45]	Unable to differentiate initial GCS13-15 patients
12.	Inamasu et al[46]	Unable to differentiate initial GCS13-15 patients
13.	Jacobs et al[47]	Includes patients no injuries on CT imaging
14.	Jiang et al[48]	Included patients of initial GCS<13 Not clear if all GCS13-15 patients have injuries present on CT imaging.
15.	Jiang et al[49]	Included patients of initial GCS<13 Not clear if all GCS13-15 patients have injuries present on CT imaging.
16.	Joseph et al[50]	Unable to differentiate initial GCS13-15 patients
17.	Joseph et al[51]	Unable to differentiate initial GCS13-15 patients
18.	Joseph et al[53]	Unable to differentiate initial GCS13-15 patients
19.	Kim et al[56]	Unable to differentiate initial GCS13-15 patients
20.	Kreitzer et al[58]	Abstract only (full study included[86])
21.	McCutcheon et al[61]	Unable to differentiate initial GCS13-15 patients
22.	Nishijima et al[64]	Abstract only and associated paper included patients of initial GCS<13
23.	Nishijima et al[67]	Unable to differentiate initial GCS13-15 patients
24.	Nishijima et al[68]	Unable to differentiate initial GCS13-15 patients
25.	Penn et al[70]	Abstract only (full study included[37])
26.	Rubino et al[72]	Outpatient Setting
27.	Orringer et al[79]	Unable to differentiate initial GCS13-15 patients
28.	Yuan et al[80]	Unable to differentiate initial GCS13-15 patients
29.	Zare et al[81]	Includes paediatric population
30.	Zhao et al[82]	Not clear about inclusion criteria and definition of non-operative-no response from authors when contacted.
31.	Park et al[83]	Unable to differentiate initial GCS13-15 patients
32.	Schuster et al[84]	Unable to differentiate initial GCS13-15 patients
33.	Smith et al[85]	Unable to differentiate initial GCS13-15 patients
34.	Choudhry et al[88]	Abstract only (full paper included[40])
35.	Tong et al[147]	Unable to differentiate initial GCS13-15 patients
36.	Yadav et al[91]	Unable to differentiate initial GCS13-15 patients and included children

37.	Cohen et al[92]	Includes patients with no injury on initial CT
38.	Stein et al[105]	Theoretical study-no data
39.	Borovich et al[110]	Case reports
40.	Knuckey et al[111]	Pre-1996
41.	Chen et al[112]	Pre-1996
42.	Mertol et al[113]	Case reports pre-1996
43.	Brown et al[115]	Unable to differentiate initial GCS13-15 patients
44.	Fainardi et al[117]	Unable to differentiate initial GCS13-15 patients
45.	Karasu et al[118]	Unable to differentiate initial GCS13-15 patients and includes children
46.	Türedi et al[120]	Includes patients with no injury on initial CT
47.	Connon et al[121]	Unable to differentiate initial GCS13-15 patients
48.	Chang et al[148]	Unable to differentiate initial GCS13-15 patients
49.	Chao et al[123]	Unable to differentiate initial GCS13-15 patients
50.	Sullivan et al[124]	Unable to differentiate initial GCS13-15 patients
51.	Innocenti et al[126]	Includes patients with no injury on initial CT
52.	Muszynski et al[127]	Includes Children
53.	Patel et al[128]	Unable to differentiate initial GCS13-15 patients
54.	Lingsma et al[129]	Includes patients with no injury on initial CT
55.	Wong et al[131]	Case studies and pre-1996
56.	Offner et al[132]	Unable to differentiate initial GCS13-15 patients
57.	Wong et al[133]	Duplicate of 55
58.	Bhau et al[134]	Unable to differentiate initial GCS13-15 patients
59.	Chen et al[39]	Includes Children and patients without CT identified injuries
60.	Gaetani et al[135]	Unable to differentiate initial GCS13-15 patients
61.	Greene et al[136]	Unable to differentiate initial GCS13-15 patients
62.	Son et al[137]	Unable to differentiate initial GCS13-15 patients
63.	Pradeep et al[138]	Unable to differentiate initial GCS13-15 patients
64.	Alahmadi et al[149]	Unable to differentiate initial GCS13-15 patients
65.	Chieregato et al[116]	Includes Children
66.	Kehoe et al[95]	Unable to differentiate initial GCS13-15 patients
67.	Lesko et al[96]	Unable to differentiate initial GCS13-15 patients
68.	Lawrence et al[94]	Includes Children
69.	Roka et al 2008[119]	Includes Children

Supplementary Material 4: Characteristics of included studies

No.	Study	Type	Size	Outcomes	Estimate of Outcome of interest	Univariate of analysis of any Prognostic factor	Multivariable Model of several prognostic factors
1	Sifri et al 2006[75]	Prospective Cohort	130	Death Neurosurgery Progression CT	✓	✓	
2	Brown et al 2007[114]	Prospective Cohort	142	Death Deterioration Neurosurgery Progression CT	✓		
3	Fabbri et al 2008[139]	Prospective Cohort	723	Death Neurosurgery	✓	✓	
4	AbdelFattah et al 2012[28]	Prospective Cohort	145	Death Deterioration Progression CT	✓		
5	Sharifuddin et al 2012[74]	Prospective Cohort	279	Death Deterioration Neurosurgery Progression CT	✓	✓	✓
6	Ding et al 2012[90]	Prospective Trial	32	Neurosurgery Progression CT	✓		
7	Nishijima et al 2014[66]	Prospective Cohort	600	Deterioration Neurosurgery	✓	✓	✓
8	Sifri et al 2004[102]	Retrospective Cohort	202	Death Deterioration Neurosurgery Progression CT	✓		
9	Velmahos et al 2006[77]	Retrospective Cohort	154	Deterioration Neurosurgery Progression CT	✓	✓	✓
10	Huynh et al 2006[97]	Retrospective Cohort	56	Deterioration Neurosurgery Progression CT	✓		
11	Bee et al 2009[99]	Retrospective Cohort	207	Death Neurosurgery	✓	✓	
12	Klein et al 2010[57]	Retrospective Cohort	323	Death Neurosurgery	✓		
13	Schaller et al 2010[8]	Retrospective Cohort	110	Death Deterioration Neurosurgery	✓		
14	Nasir et al 2011[106]	Retrospective Cross sectional	275	Neurosurgery Progression CT	✓		
15	Sifri et al 2011[125]	Retrospective Cohort	107	Deterioration Neurosurgery Progression CT	✓		

16	Levy et al 2011[59]	Retrospective Cohort SAH only	117	Death Neurosurgery Progression CT	✓		
17	Washington et al 2012[78]	Retrospective Cohort	321	Deterioration Neurosurgery Progression CT	✓	✓	✓
18	Homnick et al 2012[104]	Retrospective Cohort	341	Death Deterioration Neurosurgery Progression CT	✓		
19	Nayak et al 2013[62]	Retrospective Cohort	321	Death Neurosurgery Progression CT	✓		
20	Borczuk et al 2013[37]	Retrospective Cohort	404	Deterioration Neurosurgery	✓	✓	✓
21	Almenawer et al 2013[18]	Retrospective Cohort study and meta-analysis	445	Neurosurgery Progression CT	✓		
22	Joseph et al 2013[52]	Retrospective Cohort	270	Death Neurosurgery	✓		
23	Thorston et al 2012[6]	Retrospective Cohort	360	Neurosurgery Progression CT	✓	✓	✓
24	Choudhry et al 2013[41]	Retrospective Cohort	757	Death Deterioration Progression CT	✓	✓	✓
25	Deepika et al 2013[42]	Retrospective Cohort SAH only	34	Unable to extract			
26	Fabbri et al 2013[87]	Retrospective Cohort	1123	Progression CT	✓	✓	
27	Boris et al 2013[107]	Retrospective Cohort	68	Deterioration Neurosurgery Progression CT	✓		
28	Thomas et al 2010[7]	Retrospective Cohort	457	Deterioration Neurosurgery	✓		
29	Nishijima et al 2013[63]	Retrospective Cohort	1412	Deterioration Neurosurgery	✓		
30	Quigley et al 2013[71]	Retrospective Cohort SAH only	478	Neurosurgery Progression CT	✓		✓
31	Levy et al 2014[60]	Retrospective Cohort	76	Deterioration Neurosurgery	✓		
32	Overton et al 2014[69]	Retrospective Cohort	171	Deterioration	✓		✓
33	Phelan et al 2014[103]	Retrospective Cohort SAH only	77	Death Deterioration Neurosurgery Progression CT	✓		
34	Kreitzer et al 2014[86]	Retrospective Cohort	323	Death Neurosurgery	✓		
35	Kim et al 2014[55]	Retrospective Cohort Subdurals	98	Neurosurgery Progression CT	✓	✓	✓

		only					
36	Sweeney et al 2015[98]	Retrospective Cohort	50493	Neurosurgery	✓	✓	✓
37	Nishijima et al 2015[65]	Retrospective Cohort	151	Deterioration	✓		
38	Darby et al 2015[130]	Retrospective Cohort	369	Death Neurosurgery Progression CT	✓		✓
39	Beynon et al 2015[93]	Retrospective Cohort	70	Death Neurosurgery	✓		
40	Joseph et al 2015[54]	Retrospective Cohort	876	Neurosurgery Progression CT	✓	✓	✓
41	Ditty et al 2015[32]	Retrospective Cohort SAH/ICB only	500	Death Neurosurgery Progression CT	✓		
42	Anandalwar et al 2016[30]	Retrospective Cohort	142	Deterioration Neurosurgery	✓		
43	Bardes et al 2016[101]	Retrospective Cohort	389	Death Deterioration Neurosurgery Progression CT	✓	✓	✓
44	Shih et al 2016[100]	Retrospective Cohort	340	Deterioration Neurosurgery Progression CT	✓	✓	✓
45	Schwed et al 2016[73]	Retrospective Cohort	201	Deterioration Neurosurgery	✓	✓	✓
46	Sumritpradit et al 2016[76]	Retrospective Cohort	98	Deterioration Neurosurgery Progression CT	✓	✓	
47	Pruitt et al 2016[108]	Retrospective Cohort	1053	Deterioration Neurosurgery	✓		
48 49 50	Jospeph et al[9, 27, 109]	Three papers outlining the Brain Injury Guideline risk stratification tool and a combination of retrospective and prospective data following its implementation.					

Supplementary Material 5: Table of Risk Factors Assessed

Risk Factor		Assessed Number of studies	Univariate	Multivariate	Recursive partitioning
1 Age	Continuous	10[6, 55, 69, 71, 73, 76, 77, 98-100, 130]	7[6, 55, 73, 76, 77, 99, 100, 130]	4[69, 71, 98, 130]	
	≥65	6[37, 54, 66, 74, 77, 78]	6[37, 54, 66, 74, 77, 78]	3[54, 74, 77]	1[66]
	≥60	1[41]	1[41]	1[41]	
	≥55	2[73, 101]	1[101]	1[73]	1[101]
	≥50	1[76]	1[76]		
2 Gender		10[6, 37, 54, 55, 69, 74, 76, 77, 98, 100]	9[6, 37, 54, 55, 74, 76, 77, 98, 100]	2[54, 69]	
3 Initial GCS	<15	7[37, 41, 66, 73, 74, 77, 101]	6[37, 41, 66, 73, 74, 101]	4[37, 73, 74, 77]	2[66, 101]
	GCS	7[6, 55, 69, 73, 77, 98, 100]	4[6, 55, 73, 77, 100]	2[69, 98]	
	GCS=14	1[6]		1[6]	
	GCS=13	1[6]		1[6]	
4 CT Findings	Midline shift CT/Mass effect	5[6, 55, 66, 76, 100]	4[6, 66, 76, 100]	4[6, 55, 76, 100]	1[66]
	Marshall Classification	2[41, 73]	2[41, 73]		
	SDH>10mm	1[54]	1[54]	1[54]	
	EDH>10mm	1[54]	1[54]	1[54]	
	ICH vol>10ml	1[78]	1[78]	1[78]	
	Mean Vol	1[55]	1[55]	1[55]	
	Maximal thickness	1[55]		1[55]	
	Volume ED	1[100]	1[100]	1[100]	
	Volume SDH	1[100]	1[100]		
	Volume ICB	1[100]	1[100]		
5 Type of isolated injury	Contusion	1[37, 78]	1[37, 78]		
	SDH	3[37, 73, 98]	2[37, 73]	1[98]	
	EDH	3[37, 73, 98]	2[37, 73]	1[98]	
	SAH	3[37, 73, 98]	2[37, 73]	2[73, 98]	
	Mixed	1[73, 98]	1[73]	1[98]	
	ICB	1[73]	1[73]		
6 Presence of (includes mixed injuries)	Contusion	3[37, 76]	3[37, 76]		
	SDH	5[6, 37, 76, 100, 101]	5[6, 37, 76, 100, 101]	1[37]	
	EDH	5[6, 37, 76, 100,	5[6, 37, 76, 100,		

		101	101		
	SAH	4[6, 37, 76, 100, 101]	4[6, 37, 76, 100, 101]		
	fracture	4[6, 74, 76, 100]	4[6, 74, 76, 100]	1[100]	
	Displaced/depressed fracture	2[54, 66]	2[54, 66]	1[54]	
	Base of skull fracture	2[74, 76]	2[74, 76]		
	pneumocranium	1[100]	1[100]		
	ICB	3[6, 100, 101]	3[6, 100, 101]		
	IVH	3[6, 76, 100]	3[6, 76, 100]		
	Diffuse Axonal Injury	1[76]	1[76]		
	2+ lesions	4[6, 74, 77, 100]	4[6, 74, 77, 100]	2[74, 77]	
	3+ lesions	1[6]	1[6]		
7 Subdural with	contusion	1[55]	1[55]	1[55]	
	SAH	1[55]	1[55]	1[55]	
8 Non-isolated head Injury		1[66]	1[66]		1[66]
9 BP		7[54, 73, 76, 77, 98-100]	6[54, 73, 76, 77, 99, 100]	2[73, 98]	
10 Pre-admission Hypotension		1[66]	1[66]		
11 HR		4[54, 73, 98, 99]	3[54, 73, 99]	1[98]	
12 RR		1[98]	1[98]		
13 Pre-injury Hypoxia		1[66]	1[66]		
14 Intoxication		2[54, 55]	2[54, 55]		
15 Coagulopathy : including any anti-coagulant use		6[6, 41, 55, 77, 98, 100]	5[6, 41, 55, 77, 100]	1[98]	
16 Warfarin Use		3[37, 76, 101]	3[37, 76, 101]		
20 Warfarin or anti-platelet		2[78, 100]	2[78, 100]		
17 PT/INR		3[6, 74, 101]	3[6, 74, 101]		
18 aPPT		1[6, 101]	2[6, 101]		
19 Platelet count<100000		1[54]	1[54]	1[54]	
20 Platelet count<50000		1[55]	1[55]		
21 Hb<10		1[54]	1[54]		
22 Hb		2[74, 100]	2[74, 100]		
23 WCC		1[100]	1[100]	1[100]	
24 Aspirin		3[37, 76, 101]	3[37, 76, 101]		
25 Clopidogrel		3[37, 76, 101]	3[37, 76, 101]		
25 Any Anti-platelet		2[55, 66, 87]	1[55, 66]	1[87]	
26 ISS		11[6, 69, 71, 73, 76, 77, 98-101, 130]	9[6, 41, 73, 76, 77, 99-101, 130]	7[6, 69, 71, 73, 98, 100, 130]	
27 (H)AIS		5[41, 73, 76, 99, 101]	5[41, 73, 76, 99, 101]	1[73]	
28 LOC		1[54]	1[54]	1[54]	
29 Mechanism of Injury (unqualified)		2[54, 55]	2[54, 55]		
30 Non-fall from standing		1[66]	1[66]		
31 Fall		2[37, 77]	2[37, 77]		
32 Assault		1[37]	1[37]		
33 RTC		4[37, 74, 76, 77]	4[37, 74, 76, 77]		

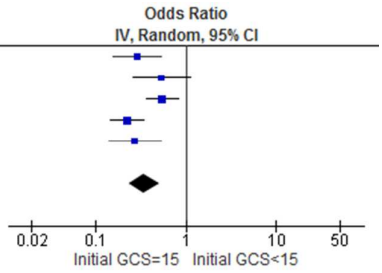
34 Pedestrian Struck		**1**[37]	**1**[37]		
35 Bicycle struck		**1**[37]	**1**[37]		
36 Lactate		**1**[54]	**1**[54]	**1**[54]	
37 Base deficit		**1**[54]	**1**[54]	**1**[54]	
38 Comorbidities	**HTN**	**3**[37, 76, 100]	**3**[37, 76, 100]		
	Diabetes	**2**[76, 100]	**2**[76, 100]		
	Old CVA	**2**[76, 100]	**2**[76, 100]		
	IHD	**2**[76, 100]	**2**[76, 100]		
	Arrhythmia	**1**[100]	**1**[100]		
	Liver disease	**1**[100]	**1**[100]		
	CKD	**1**[100]	**1**[100]		
	AKI	**1**[100]	**1**[100]		
	Any high risk	**1**[66]	**1**[66]		
39 Smoking		**1**[55]	**1**[55]		
40 Time to first CT		**2**[73, 76]	**2**[73, 76]		
41 Statin Therapy		**1**[100]	**1**[100]		

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

Study or Subgroup	Initial GCS=15 Events	Total	Initial GCS<15 Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Bardes et al 2016	31	310	22	79	18.6%	0.29 [0.16, 0.53]
Borczuck et al 2013	37	344	11	60	15.6%	0.54 [0.26, 1.12]
Fabbri et al 2008 (Neurosurgery)	62	493	47	226	24.3%	0.55 [0.36, 0.83]
Nishijima et al 2014	46	406	70	194	24.1%	0.23 [0.15, 0.35]
Schwed et al 2016	66	129	57	72	17.3%	0.28 [0.14, 0.54]
Total (95% CI)		**1682**		**631**	**100.0%**	**0.35 [0.23, 0.52]**
Total events	242		207			

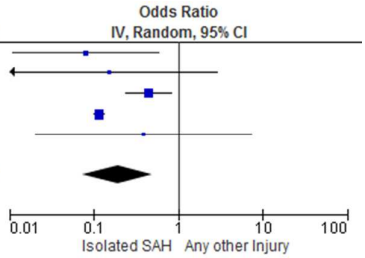
Heterogeneity: Tau² = 0.13; Chi² = 10.65, df = 4 (P = 0.03); I² = 62%
Test for overall effect: Z = 5.16 (P < 0.00001)



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

Study or Subgroup	Isolated SAH Events	Total	Any Other Injury Type Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Borczuck et al 2013	1	76	47	328	14.2%	0.08 [0.01, 0.59]
Pruitt et al 2016 (neurosurg.)	0	155	4	216	8.2%	0.15 [0.01, 2.84]
Schwed et al 2016	27	57	96	144	32.3%	0.45 [0.24, 0.84]
Sweeney et al 2015 (neurosurg.)	197	13191	4315	37305	37.2%	0.12 [0.10, 0.13]
Velmahos et al 2006 (neurosurg.)	0	33	4	121	8.2%	0.39 [0.02, 7.42]
Total (95% CI)		**13512**		**38114**	**100.0%**	**0.19 [0.07, 0.50]**
Total events	225		4466			

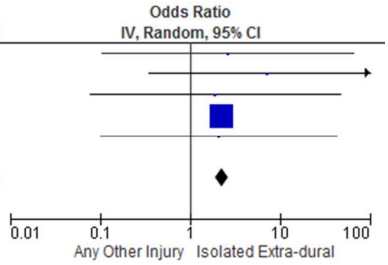
Heterogeneity: Tau² = 0.63; Chi² = 17.98, df = 4 (P = 0.001); I² = 78%
Test for overall effect: Z = 3.39 (P = 0.0007)



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

Study or Subgroup	Isolated EDH Events	Total	Any other Injury Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Borczuck et al 2013	0	1	42	378	0.3%	2.64 [0.11, 65.82]
Pruitt et al 2016 (neurosurg.)	0	5	4	366	0.3%	7.32 [0.35, 153.20]
Schwed et al 2016	1	1	122	200	0.3%	1.92 [0.08, 47.79]
Sweeney et al 2015 (neurosurg.)	159	901	4315	49595	98.8%	2.25 [1.89, 2.68]
Velmahos et al 2006 (neurosurg.)	0	7	4	144	0.3%	2.08 [0.10, 42.34]
Total (95% CI)		**915**		**50683**	**100.0%**	**2.26 [1.90, 2.68]**
Total events	160		4487			

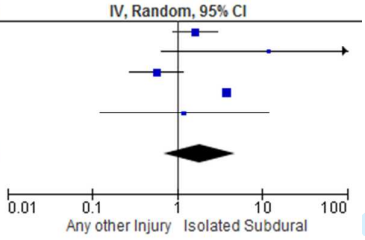
Heterogeneity: Tau² = 0.00; Chi² = 0.60, df = 4 (P = 0.96); I² = 0%
Test for overall effect: Z = 9.22 (P < 0.00001)



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

Study or Subgroup	Isolated Subdural Events	Total	Any Other Injury Events	Total	Weight	Odds Ratio IV, Random, 95% CI
Borczuck et al 2013	24	160	24	244	26.4%	1.62 [0.88, 2.96]
Pruitt et al 2016 (neurosurg.)	4	161	0	210	7.9%	12.03 [0.64, 225.05]
Schwed et al 2016	18	36	105	165	25.2%	0.57 [0.28, 1.18]
Sweeney et al 2015 (neurosurg.)	2977	18784	1497	31712	29.4%	3.80 [3.56, 4.06]
Velmahos et al 2006 (neurosurg.)	3	110	1	44	11.1%	1.21 [0.12, 11.91]
Total (95% CI)		**19251**		**32375**	**100.0%**	**1.82 [0.69, 4.77]**
Total events	3026		1627			

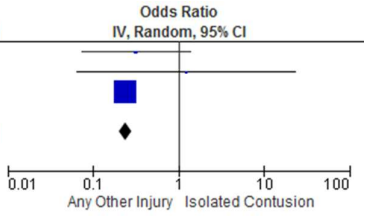
Heterogeneity: Tau² = 0.82; Chi² = 34.80, df = 4 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.21 (P = 0.23)



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

Study or Subgroup	Isolated Contus Events	Isolated Contus Total	Any Other Injury Type Events	Any Other Injury Type Total	Weight	Odds Ratio IV, Random, 95% CI
Borczuck et al 2013	2	33	46	271	1.3%	0.32 [0.07, 1.37]
Pruitt et al 2016 (neurosurg.)	0	30	4	341	0.3%	1.23 [0.06, 23.38]
Sweeney et al 2015 (neurosurg.)	139	5636	4335	44860	98.3%	0.24 [0.20, 0.28]
Total (95% CI)		**5699**		**45472**	**100.0%**	**0.24 [0.20, 0.28]**
Total events	141		4385			

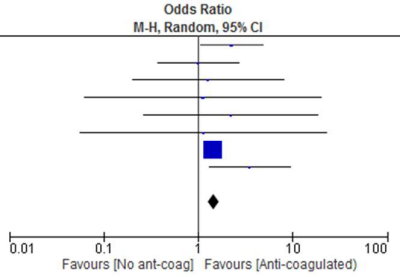
Heterogeneity: Tau² = 0.00; Chi² = 1.34, df = 2 (P = 0.51); I² = 0%
Test for overall effect: Z = 16.54 (P < 0.00001)



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

Study or Subgroup	Anti-coagulated Events	Anti-coagulated Total	Not Anti-coagulated Events	Not Anti-coagulated Total	Weight	Odds Ratio M-H, Random, 95% CI
Bardes et al 2016 (Clinical Deterioration)	11	46	42	343	2.7%	2.25 [1.06, 4.77]
Borczuck et al 2013 (Clinical Deterioration)	5	42	43	362	1.6%	1.00 [0.37, 2.69]
Kim et al 2014	2	5	32	93	0.5%	1.27 [0.20, 8.00]
Shih et al 2016 any anti-coagulant	0	10	13	330	0.2%	1.12 [0.06, 20.13]
Shih et al 2016 Warfarin or anti-platelet	1	13	12	327	0.3%	2.19 [0.26, 18.22]
Sumritpradit et al 2016	0	4	8	94	0.2%	1.13 [0.06, 22.84]
Sweeney et al 2015	279	2340	4195	48154	92.9%	1.42 [1.25, 1.61]
Thorson et al 2012	6	28	24	332	1.6%	3.50 [1.30, 9.45]
Total (95% CI)		**2488**		**50035**	**100.0%**	**1.45 [1.28, 1.64]**
Total events	304		4369			

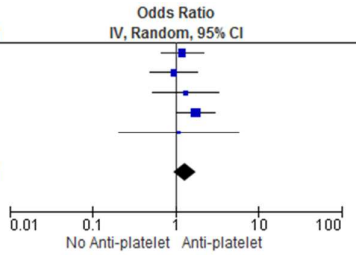
Heterogeneity: Tau² = 0.00; Chi² = 5.22, df = 7 (P = 0.63); I² = 0%
Test for overall effect: Z = 5.85 (P < 0.00001)



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

Study or Subgroup	No Anti-platelet Events	No Anti-platelet Total	Anti-platelet Events	Anti-platelet Total	Weight	Odds Ratio IV, Random, 95% CI
Bardes et al 2016 Aspirin	23	154	30	235	28.3%	1.20 [0.67, 2.16]
Borczuck et al 2013 Aspirin	15	130	33	274	23.1%	0.95 [0.50, 1.82]
Kim et al 2014 (neurosurg.)	11	28	23	70	11.8%	1.32 [0.53, 3.28]
Nishijima et al 2014	22	79	94	521	33.3%	1.75 [1.02, 3.01]
Sumritpradit et al 2016 Aspirin (neurosurg.)	2	23	6	75	3.5%	1.10 [0.21, 5.84]
Total (95% CI)		**414**		**1175**	**100.0%**	**1.30 [0.95, 1.78]**
Total events	73		186			

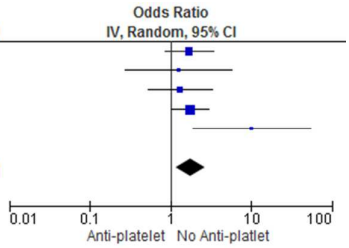
Heterogeneity: Tau² = 0.00; Chi² = 2.17, df = 4 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.66 (P = 0.10)



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

Study or Subgroup	Anti-platelet Events	Anti-platelet Total	No Anti-platelet Events	No Anti-platelet Total	Weight	Odds Ratio IV, Random, 95% CI
Bardes et al 2016 Clopidogrel	13	67	40	322	28.4%	1.70 [0.85, 3.38]
Borczuck et al 2013 Clopidogrel	2	14	46	390	7.1%	1.25 [0.27, 5.75]
Kim et al 2014 (neurosurg.)	11	28	23	70	18.2%	1.32 [0.53, 3.28]
Nishijima et al 2014	22	79	94	521	40.5%	1.75 [1.02, 3.01]
Sumritpradit et al 2016 Clopidogrel (neurosurg.)	3	8	5	90	5.8%	10.20 [1.88, 55.38]
Total (95% CI)		**196**		**1393**	**100.0%**	**1.79 [1.17, 2.72]**
Total events	51		208			

Heterogeneity: Tau² = 0.04; Chi² = 4.73, df = 4 (P = 0.32); I² = 15%
Test for overall effect: Z = 2.71 (P = 0.007)



Supplementary Material 7: Pooled risk of clinical deterioration stratified by the injury type identified by initial CT imaging