Performance of the Hull Salford Cambridge Decision Rule (HSC DR) for early discharge of patients with findings on CT scan of the brain: a CENTER-TBI validation study

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ABSTRACT

Background There is international variation in hospital admission practices for patients with mild traumatic brain injury (TBI) and injuries on CT scan. Only a small proportion of patients require neurosurgical intervention, while many guidelines recommend routine admission of all patients. We aim to validate the Hull Salford Cambridge Decision Rule (HSC DR) and the Brain Injury Guidelines (BIG) criteria to select low-risk patients for discharge from the emergency department.

Method A cohort from 18 countries of Glasgow Coma Scale 13–15 patients with injuries on CT imaging was identified from the multicentre Collaborative European NeuroTrauma Effectiveness Research in TBI (CENTER-TBI) Study (conducted from 2014 to 2017) for secondary analysis. A composite outcome measure encompassing need for ongoing hospital admission was used, including seizure activity, death, intubation, neurosurgical intervention and neurological deterioration. We assessed the performance of our previously derived prognostic model, the HSC DR and the BIG criteria at predicting deterioration in this validation cohort.

Results Among 1047 patients meeting the inclusion criteria, 267 (26%) deteriorated. Our prognostic model achieved a C-statistic of 0.81 (95% CI: 0.78 to 0.84). The HSC DR achieved a sensitivity of 100% (95% CI: 97% to 100%) and specificity of only 4.7% (95% CI: 3.3% to 6.5%) for deterioration. Using the BIG criteria for discharge from the ED achieved a higher specificity (13.3%, 95% CI: 10.9% to 16.1%) and lower sensitivity (94.6%, 95% CI: 90.5% to 97%), with 12/105 patients recommended for discharge subsequently deteriorating, compared with 0/34 with the HSC DR.

Conclusion Our decision rule would have allowed 3.5% of patients to be discharged, none of whom would have deteriorated. Use of the BIG criteria may select patients for discharge who have too high a risk of subsequent deterioration to be used clinically. Further validation and implementation studies are required to support use in clinical practice.

BACKGROUND

Over 2 million patients are admitted to hospital each year across Europe for traumatic brain injury (TBI; injury to the brain or alteration of brain function due to external force).1 Overall, 95% of patients admitted to hospital and 36% of patients admitted to intensive care units with TBI have an initial Glasgow Coma Scale (GCS) of 13–15 and are defined as having mild injuries.2 The management of mild TBI patients with injuries identified by CT imaging is controversial.

Around 7% of initial GCS 13–15 patients who present with head trauma have intracranial injuries or skull fractures identified on CT imaging but only around 1% of patients die or require neurosurgery.3 Some studies advocate routine admission under specialist neurosurgical care and repeat CT imaging of all mild TBI patients with injuries identified on CT imaging.4 Some North American centres have adopted the consensus derived Brain Injury Guidelines (BIG) criteria which advocates the discharge of selected low-risk patients with traumatic brain injuries identified by CT imaging.

What is already known on this subject

National Institute for Health and Care Excellence (NICE) head injury guidelines state that following head injury, patients with ‘new, clinically significant abnormalities on imaging’ should be admitted for observation without defining which injuries are clinically significant. We have previously empirically derived the first prognostic model and decision rule (Hull Salford Cambridge Decision Rule (HSC DR)) to identify low-risk patients with injuries on CT imaging who could be safely discharged from the Emergency Department (ED).

What this study adds

We present the first validation study of our prognostic model and the HSC DR. It shows that application of the HSC DR may allow a modest but safe reduction in inpatient admissions of selected low-risk patients with traumatic brain injuries identified by CT imaging.
predicting need for hospital admission in this population.\textsuperscript{7} We compared the performance of the HSC DR and BIG criteria and found both had high sensitivity to clinical deterioration. The HSC DR maximised sensitivity at a cost of a specificity of 7\% at the discharge threshold to ensure clinical safety, but implementation would have recommended fewer than 1 in 10 patients with TBI be discharged.\textsuperscript{7} However, in the ‘COVID-19’ era, reducing hospital-acquired infections is paramount, and in other resource constrained contexts, even small reductions in unnecessary hospital admissions are valuable. Application of this decision rule could—if externally validated—achieve this.\textsuperscript{7}

The aims of this study were:

1. Externally validate and compare the performance of the HCS and BIG criteria decision rules, using an international dataset of patients attending emergency departments following TBI.
2. Evaluate the performance of the HCS and BIG criteria decision rules for mildly injured patients with TBI.
3. Externally validate the empirically derived prediction model underpinning HSC DR (recalibrating where required) using the CENTER-TBI cohort.

**METHODS**

**Study design**

An international dataset of patients with CT diagnosed TBI was used to externally validate the two decision rules (BIG and HSC DR) by comparing their sensitivity and specificity for predicting which patients required hospital admission for specific treatments.\textsuperscript{2,8} The CENTER-TBI dataset was then used to recalibrate the HSC prediction model (which then feeds into the decision rule). The aim of the recalibration was to determine if the HSC DR performance could be improved using data from a more diverse population compared with the initial derivation dataset. We followed international guidelines (TRIPOD) for reporting of prognostic model validation.\textsuperscript{8} The methods used to derive our prognostic model and the HSC DR are available in the previously published protocol and derivation studies.\textsuperscript{7,9}

**Source of data**

Data for the core CENTER-TBI Study were collected between December 2014 and December 2017 at 63 centres across Europe and Israel and 4509 patients of all TBI severity were recruited, stratified by three strata of planned clinical management: ED only, admitted initially as a ward inpatient and admitted initially to intensive care. All patients were initially managed in the emergency department. Data were prospectively collected by trained research staff as detailed in the study protocol.\textsuperscript{10} Follow-up data were collected at 2–3 weeks, 3 months and 6 months with data collected on 83.4\% of patients at 6 months.

**Inclusion and exclusion criteria**

Patients aged 16 years and over with an initial GCS 13–15 recorded in the ED and with either a skull fracture, intracranial haemorrhage or cerebral contusion identified on first CT scan—regardless of care pathway stratum—were included, reflecting the population used in our derivation study.\textsuperscript{7} Patients whose initial GCS in the ED was unknown and patients whose diffuse axonal injury was the sole injury identified on initial CT scan were excluded.

**Outcome**

A composite outcome encompassing need for hospital admission was defined, matching the outcome in the model derivation study. This included: seizure as inpatient or at 2-week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to intensive care (ICU) for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration (new deficit or drop in GCS of more than 1 point).

**Predictors**

The original extended prediction model includes seven predictor variables for a composite outcome of deterioration encompassing need for hospital admission in this TBI population (table 1).\textsuperscript{7} The full prediction model is available in online supplemental material 2. Six of these variables were used in our derivation study to form the simplified HSC DR which could be applied clinically to identify patients who could be safely discharged from the ED (table 1, online supplemental material 2). The BIG criteria use six factors to risk stratify patient management (online supplemental material 1). All factors in the prediction model and BIG criteria were available from data collected in CENTER-TBI.

**Sample size**

A minimum of between 100–200 events and 100–200 non-events per study sample have been recommended for validation studies of logistic regression models.\textsuperscript{11,12} The validation cohort contained over 200 events and non-events.

**Missing data**

To evaluate model performance, missing data were multiply imputed using the ICE STATA package on the assumption they were missing at random (fully described in online supplemental material 3).\textsuperscript{13} Performance was averaged across imputed data sets.\textsuperscript{14,15}

**Decision rule performance**

All analyses were completed using STATA V.16 (StataCorp LLC, College Station, Texas). Sensitivity and specificity of the HSC DR and of the BIG criteria to the composite outcome of

| Table 1 | Factors in extended prognostic model, HSC DR and BIG criteria |
|---------|-------------------------------------------------------------|
| **Factors in extended model** | **HSC DR** | **BIG criteria** |
| **If discharged** | **If discharged after 6 hours** |
| Preinjury anticoagulation or antiplatelets | No | No |
| Initial GCS 13–15 | GCS 15 | 13–15 |
| First neurological examination | Normal | Normal |
| Number of injuries on CT: 1–5 or diffuse | 1 | |
| Injury severity on CT: | Simple skull fracture | Subdural ≤4 mm |
| | Simple skull fracture or 1–2 bleeds <5 mm total | Extradural ≤4 mm |
| | Complex skull fracture | 1 intracerebral |
| | Marshall Ila 1–2 bleeds <5 mm (total) | haemorrhage ≤4 mm |
| | Marshall IIb bleeds ≥5 mm | Trace subarachnoid |
| | Marshall III/IV | haemorrhage |
| | Marshall IV | No skull fractures |
| | Brain stem/cerebellar | No intraventricular haemorrhage |
| Injury Severity Score (body regions excluding head) | Up to two non-significant extracranial injuries (not requiring impatient care, eg. closed fracture humerus) | |
| Intoxication | Not intoxicated | |
| Haemoglobin | Not included in risk score | |
deterioration were calculated in patients with complete data for either criteria. To be recommended for discharge, all components of HSC DR or BIG criteria (table 1) must be fulfilled. The proportion of patients recommended for discharge and accompanying risk of deterioration in a discharged patient (negative predictive value) were compared. In prespecified exploratory subgroup analysis, this was repeated in patients with less severe injuries as indicated by having a brain Abbreviated Injury Score (AIS) or Marshall classification <3.16 This represents patients without obvious midline shift or severe injuries on CT imaging and the population admitted for observation under ED care in the UK.

Model performance and recalibration
Performance of the prediction model was assessed in the CENTER-TBI cohort using measures of discrimination and calibration. Discrimination indicates how well the model differentiates between patients who deteriorated and those who do not deteriorate and was measured using the C-statistic (equivalent to the area under the receiver operator characteristic curve).17

Calibration measures how closely predictions made by the model match observed outcomes (ie, do predicted mean outcomes match observed mean outcomes).17 Calibration was assessed visually using a calibration plot and with estimates of the ‘calibration in the large’ (the ratio of expected vs observed numbers of events) and slope of the calibration plot (the overall prognostic effects of predictors in the model). To account for differences between the derivation and validation cohort and potential model over-fitting during derivation, the intercept and coefficients of the prediction model were also re-estimated to provide a recalibrated model.

Clinical usefulness
Decision curve analysis was used to estimate the net benefit of using the prognostic model to select patients for discharge from the ED.1819 Net benefit is estimated by the number of true positives minus false positives multiplied by the clinical weight given to correct classification across a range of probabilities of deterioration where discharge could be considered.19 The net benefit of using the prognostic model was compared visually in curves using the BIG criteria’s single decision threshold and reference strategies of discharging no or all patients.20

Patient and public involvement
The Hull and East Yorkshire NHS Trust Trans-Humber Consumer Research Panel and Hull branch of the Headway charity helped inform developing the overall research aim of developing a predictive model to identify low-risk patients with injuries on CT imaging who could be safely discharged from the ED.

RESULTS
Study population
The cohort (n=1047) had mostly male, with over a third of patients aged over 65 and over 20% with either preinjury anti-coagulant or antiplatelet use (figure 1, table 2). A total of 379 (36%) patients had data missing from at least one predictor variable value (mostly initial haemoglobin) used in the full prognostic model (table 2). Overall, 12.1% patients had data missing in one or more predictor variable used in the HSC DR. Any clinical deterioration was noted among 267 patients (26%; 95% CI: 23% to 28%), including 212 patients (20%; 95% CI: 17.8% to 23%) who underwent neurosurgery, died or were intubated and 25 patients had deaths attributable to TBI.

Figure 1 Strengthening the Reporting of Observational Studies in Epidemiology flow diagram of selection of study population. GCS, Glasgow Coma Scale; TBI, traumatic brain injury; CENTER-TBI, Collaborative European NeuroTrauma Effectiveness Research in TBI; DAI, Diffuse Axonal Injury.

Decision rule performance
The HCS DR achieved a sensitivity of 100% (95% CI: 98.8% to 100%), but very low specificity of 4.7% (95% CI: 3.3% to 6.5%) for the composite outcome of deterioration (table 3). BIG 1 classification missed some events (sensitivity 94.6%, 95% CI: 90.5% to 97%), but had higher specificity (13.3%, 95% CI: 10.9% to 16.1%). Application of the HSC DR would have recommended discharge of only 3.5% of patients, compared with 11.4% patients recommended by the BIG criteria. However, patients recommended for discharge by the BIG criteria had a 11.4% (95% CI: 6.7% to 18.9%) risk of subsequent deterioration compared with 0% (95% CI: 0% to 10.2%) of the HSC DR.

Subgroup analysis of less severely injured patients
One hundred and forty-six patients had AIS <3 and 800 patients had Marshall classification <3 injuries. Use of the HSC DR would have facilitated discharge of 23% (34/146) of patients with brain AIS <3 and 4.23% (34/800) of patients with Marshall classification <3 injuries.

No patients selected for discharge by the HSC DR deteriorated (risk of deterioration 0%, 95% CI: 0% to 10.2%). Use of BIG criteria would have selected 26% (37/142) of patients with brain AIS <3 injuries for discharge but with an 8.1% (95% CI: 2.8% to 21.3%) risk of deterioration and 13.6% (105/770) of patients with Marshall classification <3 injuries but with an 11.4% (95% CI: 6.7% to 18.9%) risk of deterioration (table 4, online supplemental material 6).

Twenty-seven patients were excluded from the cohort as the only injury identified on initial CT imaging was diffuse axonal injury and therefore, they could not be assigned to a BIG
Original research

Table 2  Characteristics of the study population (N=1047)

| Population characteristic | Category                        | Mean (SD), min–max or N (%) | Missing data |
|----------------------------|---------------------------------|-------------------------------|--------------|
| Age                        | Years                           | 54.8 (SD=19.7)               | None         |
|                           | 16–96                            | 16–96                         | None         |
| Age ≥65                    |                                 | 384 (36.7%)                  | None         |
| Sex                        | Male                             | 688 (66%)                    | None         |
|                           | Female                           | 359 (34%)                    | None         |
| GCS                        | 15                               | 677 (64.7%)                  | None         |
|                           | 14                               | 359 (24.7%)                  | None         |
|                           | 13                               | 111 (10.6%)                  | None         |
| Stratum                    | Emergency Department Admission   | 87 (8.3%)                    | None         |
|                           | Intensive Care Unit              | 587 (56%)                    | None         |
|                           | 373 (35.6%)                     |                              |              |
| Mechanism of injury        | High velocity trauma             | 210 (20.1%)                  | 33 (3.2%)    |
|                           | Blow to head/struck by object    | 183 (17.5%)                  |              |
|                           | Ground level fall                | 384 (36.7%)                  |              |
|                           | Fall from >1 m or 5 stairs       | 218 (20.8%)                  |              |
|                           | Other                            | 19 (1.8%)                    |              |
| Intoxicated                | Yes                              | 242 (23.1%)                  | 58 (5.5%)    |
| Preinjury anticoagulation or antiplatelets | Anticoagulation use     | 72 (6.9%)                    | 12 (1.1%)    |
|                           | Antiplatelet use                 | 134 (12.8%)                  |              |
|                           | Both                             | 7 (0.7%)                     |              |
| Abnormal first neurological examination | Yes                          | 152 (14.5%)                  | 71 (6.8%)    |
| Haemoglobin                | g/L                              | 135 (SD 19.9)                | 325 (31%)    |
|                           | 47–23.4                          |                              |              |
| Number of injuries on CT   | 1                                | 468 (44.7%)                  | None         |
|                           | 2                                | 243 (23.2%)                  |              |
|                           | 3                                | 135 (12.9%)                  |              |
|                           | 4                                | 81 (7.7%)                    |              |
|                           | 5                                | 56 (5.4%)                    |              |
|                           | Multiple diffuse injury>5        | 64 (6.1%)                    |              |
| Injury severity on CT (modified Marshall classification described in detail Online supplemental material 2) | 1. Simple skull fractures | 19 (1.8%) | None |
|                           | 2. Complex skull fractures       | 67 (6.4%)                    |              |
|                           | 3. 1–2 bleeds <5 mm (total)      | 426 (40.7%)                  |              |
|                           | 4. No or minimal mass effect     | 324 (31%)                    |              |
|                           | 5. Significant midline shift     | 29 (2.8%)                    |              |
|                           | 6. High-density/mixed-density lesion | 114 (10.9%)               |              |
|                           | 7. Cerebellar/brain stem injury  | 68 (6.5%)                    |              |
| Injury Severity Score      | Body regions excluding head      | 17.3 (SD 20.6)               | 9 (0.9%)     |
|                           | 1–15 (range)                    |                              |              |

GCS, Glasgow Coma Scale.

criterion. These injuries are equivalent to a Marshall score 4 severity and would be recommend for admission by the HSC DR. Sensitivity analysis including these patients found the HSC DR achieved a sensitivity (100%–95% CI: 98% to 100%) and specificity (4.5%–95% CI: 3.2% to 6.3%) to the composite outcome of deterioration.

Model performance

The original prognostic model achieved a C-statistic of 0.81 (95% CI: 0.78 to 0.84) in the CENTER-TBI cohort (0.75 in the development cohort) and an estimated slope of the calibration plot of 0.51 in the CENTER-TBI cohort (0.86 in the development cohort) (figure 2A). The effect of recalibration of both the intercept and coefficients is presented in figure 2B and the recalibrated model is presented in online supplemental material 7. Measures of calibration improved but the estimated C-statistic of the recalibrated model remained 0.81.

Clinical usefulness, analysis according to clinical tolerance for adverse outcomes

Clinical usefulness depends on tolerance of risk of deterioration in those discharged without observation. Figure 3 presents the decision curves and net benefit analysis for the selection of patients either for a period of inpatient hospital observation or discharge directly from the ED using the recalibrated prognostic model or BIG criteria in the CENTER-TBI cohort. Due to the high risk of harm associated with discharging a patient who subsequently deteriorates, the analysis was limited to those with a low predicted probability of deterioration. Use of our recalibrated model showed potential benefit over an ‘admit-all’ strategy if the threshold for the predicted probability of deterioration was over 2% (figure 3), which is potentially an acceptable clinical risk of deterioration in a discharged patient. If 2% is considered too high a risk to discharge a patient, given the harm associated with deterioration in the community, then no net benefit over an ‘admit-all’ strategy was demonstrated. The BIG criteria showed benefit over an ‘admit-all’ strategy up to a threshold for predicted probability of deterioration of around 12%.

DISCUSSION

Summary

This study validated the performance of the BIG and HSC DRs in a large international dataset of patients with TBI, who had an overall deterioration prevalence of 26% (95% CI: 23% to 28%). The BIG criteria achieved a sensitivity of 94.6% (95% CI: 90.5% to 97%)
and specificity of 13.3% (95% CI: 10.9% to 16.1%) and would have recommended discharge of 11% of patients with an accompanying risk of subsequent deterioration of 11.4% (95% CI: 6.7% to 18.9%). The HSC DR achieved a sensitivity of 100% (95% CI: 98% to 100%) and specificity of 4.7% (95% CI: 3.3% to 6.5%), comparable to that reported in the development cohort (99.5% and 4.8%, respectively). The HSC DR would have recommended discharge of 3.5% of patients but with a subsequent risk of deterioration of 0% (95% CI: 0% to 10.2%). The prognostic model that underpins the HSC DR achieved a C-statistic of 0.81 and recalibration improved accuracy of individual predicted risk of deterioration (calibration).

In the subgroup of patients with less severe injuries who are more likely admitted under non-specialist teams, the BIG criteria recommended discharge of 26% of patients with brain AIS <3 injuries for discharge but with an 8.1% (95% CI: 2.8% to 21.3%) risk of deterioration. The HSC DR recommended discharge of 23% of patients in this group with a risk of subsequent deterioration of 0% (95% CI: 0% to 10.2%).

### Strengths
This study is the first external validation of the HSC DR and, alongside our previous development study, is the largest study to externally validate the BIG criteria and only study to do so in a multicentre European cohort of patients. The CENTER-TBI Study has good prospective patient follow-up and so significant adverse outcomes in the community were unlikely to have been missed. We have adhered to international guidelines for model validation. We explicitly addressed the potential clinical usefulness of the decision rule and prognostic model according to a range of potential thresholds. This decision curve analysis clarified that if quite low risks were already considered too high, for example, corresponding to a threshold of 1%, a treat all strategy would dominate. On the other hand, a less risk averse clinical policy, such as accepting risks up to 10% as acceptable, would lead to greater value of our rule or model (figure 3).

### Table 3  Performance of BIG and HSC DRs*

| BIG criteria performance | N=921 | Deteriorated | Did not deteriorate | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|--------------------------|-------|--------------|---------------------|-------------|-------------|--------------------------|--------------------------|
| BIG 1 (discharge from Emergency Department after 6 hours) | 12 | 93 | 94.6% (90.5%–97%) | Negative predictive value 88.6% (80.5%–93.7%) |
| BIG 2/3 (admit) | 210 | 606 | Specificity 13.3% (10.9%–16.1%) | Positive predictive value 25.7% (22.8%–28.9%) |

| HSC DR | N=961 | Deteriorated | Did not deteriorate | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|--------|-------|--------------|---------------------|-------------|-------------|--------------------------|--------------------------|
| Risk=0 (discharge) | 0 | 34 | 100% (988%–100%) | Negative predictive value 100% (87.4%–100%) |
| Risk >0 (admit) | 234 | 693 | Specificity 4.7% (3.3%–6.5%) | Positive predictive value 25.2% (22.5%–28.2%) |

Table 3  Performance of BIG and HSC DRs*

*Full performance of the BIG is presented in online supplemental material 4 and characteristics of patients recommended for discharge in online supplemental material 5.

BIG, Brain Injury Guidelines; HSC DR, Hull Salford Cambridge Decision Rule.

### Table 4  Subgroup analysis AIS <3

| BIG 1 | N=142 | Deteriorated | Did not deteriorate | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|-------|-------|--------------|---------------------|-------------|-------------|--------------------------|--------------------------|
| BIG 1 (discharge from Emergency Department after 6 hours) | 3 | 34 | 75% (42.8%–93.3%) | Negative predictive value 91.9% (77%–97.9%) |
| BIG 2/3 (admit) | 9 | 96 | Specificity 26.2 (19%–34.7%) | Positive predictive value 8.6% (4.2%–16.1%) |

| HSC DR | N=146 | Deteriorated | Did not deteriorate | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|--------|-------|--------------|---------------------|-------------|-------------|--------------------------|--------------------------|
| Risk=0 (discharge) | 0 | 34 | 100% (69.99%–100%) | Negative predictive value 100% (87.4%–100%) |
| Risk >0 (admit) | 12 | 100 | Specificity 25.4% (18.4%–33.8%) | Positive predictive value 10.7% (107.9%–18.313%) |

AIS, Abbreviated Injury Score; BIG, Brain Injury Guidelines; HSC DR, Hull Salford Cambridge Decision Rule.

Figure 2  Slope of the calibration plot of original and recalibrated prognostic model. EO, Expected:Observed; CITL, Calibration in The Large; AUC, Area Under the Curve.
Comparison to previous literature
In the CENTER-TBI cohort, 20% of patients underwent neurosurgery, died or were intubated compared with 13.1% in our development cohort and had a higher prevalence of deterioration than reported in a previous systematic review.4 This may reflect recruitment of more severely injured patients to the CENTER-TBI Study.

The BIG criteria for discharging patients from the ED achieved a lower sensitivity (94.6%) and higher specificity (13.3%) than when applied to our development cohort (sensitivity 99.5% and specificity 4.8%). Application of the BIG criteria would have allowed 11.4% of patients to be discharged from the ED which is similar to the 10% of patients estimated in studies conducted where the BIG criteria was developed in the USA and 15% reported in an external validation study.6,21,23 The derivation and validation studies reported by the team that developed the BIG criteria and available external validation studies report no adverse outcomes in patients recommended for discharge by the BIG criteria.6,21-23,26 In the CENTER-TBI cohort, patients recommended for discharge had a 11.4% (95% CI: 6.7% to 18.9%) risk of subsequently deteriorating. This may reflect the broader composite outcome measure used in our study and more comprehensive prospective follow-up of patients for deterioration. Some validation studies also modified the BIG criteria so that any patient with an initial GCS<15 was admitted to hospital.25 The USA TBI population used for these studies also appears to be at lower risk with a lower reported average age, anticoagulant use and neurological intervention rate.4,23 The risk of deterioration when discharging a patient from the ED that is acceptable to patients and clinicians is subjective. When deriving the HSC DR,4 we aimed to maximise sensitivity and aimed for a risk of a discharged patient deteriorating of around 1%, as this corresponds to other decision rules for discharging patients from the ED,25,27 and may be a sufficiently low risk to consider routine discharge. However, significant variation in risk tolerance in clinicians and public representatives has been demonstrated, with some indicating that even a 1% risk of deterioration may be too high.28,29

Implications
There is variation internationally in management and admission practices in this TBI population.4 In the UK and other European countries, guidelines recommend admission of all patients with TBI identified on CT imaging. This validation study shows a recalibrated version of our prognostic model could allow accurate prediction of risk of deterioration, and application of the HSC DR would have allowed a modest but safe reduction in hospital admissions for this group. The application of the BIG criteria would have discharged more patients but with a higher risk of subsequent deterioration in this European population, which may not be clinically acceptable. As indicated by our exploratory subgroup analysis, application of the HSC DR may be more beneficial when applied to lower risk populations more reflective of patients who attend the ED and are admitted for observation under emergency medicine or other non-neurosurgical specialities in the UK.

Our net benefit analysis using decision curves (figure 3) showed use of our prognostic model may show benefit over an ‘admit-all’ strategy if the threshold for the predicted probability of deterioration was over 2% and patients selected for discharge by the HSC DR had a 0% (95% CI: 0% to 10.2%) risk of deterioration. This may be sufficiently low risk to use routinely. Research is needed to assess clinician and patient risk appetite in this population and assess the clinical impact of implementing the HSC DR where patient circumstances such as intoxication or social circumstances may further affect whether a patient can be discharged. Research to improve the accuracy of the prognostic model (eg, through including biomarkers, other novel prognostic factors or better classification of injury severity on CT imaging) is also needed.

Conclusion
Use of the HSC DR would allow a modest but safe reduction in hospital admissions for mild TBI patients with injuries identified on CT imaging. The BIG criteria appear to result in an unacceptably high risk of subsequent deterioration (1 in 10) among discharged patients. Future research should further

Figure 3 Decision curve analysis. BIG, Brain Injury Guidelines.
validate our prognostic model and the HSC DR, consider safe implementation into clinical practice and assess whether inclusion of novel prognostic factors could improve the specificity of the model allowing more patients to be safely discharged.

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REFERENCES
1 Majdan M, Plancikova D, Brazinova A, et al. Epidemiology of traumatic brain injuries in Europe: a cross-sectional analysis. Lancet Public Health 2016;1:66–83.
2 Steyerberg EW, Wiegars E, Sewall C, et al. Case-Mix, care pathways, and outcomes in patients with traumatic brain injury in CENTER-TBI: a European prospective multicentre, longitudinal, cohort study. Lancet Neurol 2019;18:923–34.
3 Hayden MJ, Preston CA, Mills TJ, et al. Indications for computed tomography in patients with minor head injury. N Engl J Med 2000;343:100–5.
4 Marincowitz C, Lecky FE, Townsend W, et al. The risk of deterioration in GCS13–15 patients with traumatic brain injury identified by computed tomography imaging: a systematic review and meta-analysis. J Neurotrauma 2018;35:703–18.
5 Thomas BW, Mejia VA, Maxwell RA, et al. Scheduled repeat CT scanning for traumatic brain injury remains important in assessing head injury progression. J Am Coll Surg 2010;210:824–30.
6 Joseph B, Fries RS, Sadoun M, et al. The (big brain injury guidelines) project: defining the management of traumatic brain injury by acute care surgeons. J Trauma Acute Care Surg 2014;76:965–9.
7 Marincowitz C, Lecky FE, Allgar V, et al. Development of a clinical decision rule for the early safe discharge of patients with mild traumatic brain injury and findings on computed tomography brain scan: a retrospective cohort study. J Neurotrauma 2020;37:324–33.
8 Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD). Ann Intern Med 2015;162:735–6.
9 Marincowitz C, Lecky FE, Townsend W, et al. A protocol for the development of a prediction model in mild traumatic brain injury with CT scan abnormality: which patients are safe for discharge? Diagn Progn Res 2016;2:6.
10 Maas AIR, Menon DK, Steyerberg EW, et al. Collaborative European neurotrauma effectiveness research in traumatic brain injury (CENTER-TBI): a prospective longitudinal observational study. Neurosurgery 2015;76:67–80.
11 Vergouwe Y, Steyerberg EW, Eijkemans MJC, et al. Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. J Clin Epidemiol 2005;58:875–83.
12 Collins GS, Ongurdu EO, Altman DG. Sample size considerations for the external validation of a multivariable prognostic model: a resampling study. Stat Med 2016;35:214–26.
13 Royston P, White I. Multiple imputation by Chained Equations (MICE): Implementation in Stata. J Stat Softw 2011;45:1–20.
14 Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009;339:b2393.
15 Nguyen CD, Carlin JB, Lee KJ. Model checking in multiple imputation: an overview and case study. Emerg Themes Epidemiol 2017;14:8.
16 Association for the Advancement of Automotive Medicine. Abbreviated injury scale: 2015 revision. 6th edn. Chicago, IL, 2018.
17 Steyerberg EW, Vickers AI, Cook NR, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. Epidemiology 2010;21:128–38.
18 Vickers AI, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making 2006;26:565–74.
19 Steyerberg EW, Vergouwe Y. Towards better clinical prediction models: seven steps for development and an ABCD for validation. Eur Heart J 2014;35:1925–31.
20 Vickers AI, Van Calster B, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests. BMJ 2016;352:i6.
21 Ross M, Pang PS, Raslan AM, et al. External retrospective validation of brain injury guidelines criteria and modified guidelines for improved care value in the management of patients with low-risk neurotrauma. J Neurosurg 2019;133:1–6.
22 Capron GK, Voights MB, Moore HR, et al. Not every trauma patient with a radiographic head injury requires transfer for neurosurgical evaluation: application of the brain injury guidelines to patients transferred to a level 1 trauma center. Am J Surg 2017;214:1182–5.
23 Joseph B, Azz H, Pandit V, et al. Prospective validation of the brain injury guidelines: managing traumatic brain injury without neurosurgical consultation. J Trauma Acute Care Surg 2014;77:984–8.
24 Bahler J, Arikian F, Pedraza S, et al. Reliability of clinical guidelines in the detection of patients at risk following mild head injury: results of a prospective study. J Neurosurg 2004;100:825–34.
25 Stiel IG, Wells GA, Vandenheuvel K, et al. The Canadian CT head rule for patients with minor head injury. Lancet 2001;357:1391–6.
26 Azim A, Jehan FS, Rhee E, et al. Big for small: validating brain injury guidelines in pediatric traumatic brain injury. J Trauma Acute Care Surg 2017;83:1200–4.
27 Battle C, Hutchings H, Lovett S, et al. Predicting outcomes after blunt chest wall trauma: development and external validation of a new prognostic model. Crit Care 2014;18:R98.
28 Than M, Herbert M, Flaws D, et al. What is an acceptable risk of major adverse cardiac event in chest pain patients soon after discharge from the emergency department?: a clinical survey. Int J Cardiol 2013;166:752–4.
29 O’Keeffe ST. A cross-sectional study of doctors’, managers’ and public representatives’ views regarding acceptable level of risk in discharges from the emergency department. QJM 2015;108:533–8.