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# Stockholm score of lesion detection on computed tomography following mild traumatic brain injury (SELECT-TBI): study protocol for a multicentre, retrospective, observational cohort study

Alexander Fletcher-Sandersjöö [ID] ,[1,2] Charles Tatter,[1,2] Li Yang,[3,4] Emeli Pontén,[5] Magnus Boman,[6,7] Philipp Lassarén [ID] ,[2] Sune Forsberg,[8] Ingrid Grönlund,[9] Viktor Tidehag,[9] Rebecka Rubenson-Wahlin,[3,4] Lovisa Strömmer,[10,11] Karin Westberg,[9] Kristian Ängeby,[3,4] Therese Djärv [ID] ,[12] Olof Lundblad,[12] Jiri Bartek Jr,[1] Eric Peter Thelin [ID] [2]

## ABSTRACT

**Introduction** Mild traumatic brain injury (mTBI) is one of the most common reasons for emergency department (ED) visits. A portion of patients with mTBI will develop an intracranial lesion that might require medical or surgical intervention. In these patients, swift diagnosis and management is paramount. Several guidelines have been developed to help direct patients with mTBI for head CT scanning, but they lack specificity, do not consider the interactions between risk factors and do not provide an individualised estimate of intracranial lesion risk. The aim of this study is to create a model that estimates individualised intracranial lesion risks in patients with mTBI who present to the ED.

**Methods and analysis** This will be a retrospective cohort study conducted at ED hospitals in Stockholm, Sweden. Eligible patients are adults (≥15 years) with mTBI who presented to the ED within 24 hours of injury and performed a CT scan. The primary outcome will be a traumatic lesion on head CT. The secondary outcomes will be any clinically significant lesion, defined as an intracranial finding that led to neurosurgical intervention, hospital admission ≥48 hours due to TBI or death due to TBI. Machine-learning models will be applied to create scores predicting the primary and secondary outcomes. An estimated 20 000 patients will be included.

**Ethics and dissemination** The study has been approved by the Swedish Ethical Review Authority (Dnr: 2020-05728). The research findings will be disseminated through peer-reviewed scientific publications and presentations at international conferences.

**Trial registration number** NCT04995068.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This will be the first study to assess the interactions between risk factors, both in terms of synergism and antagonistic effects, to provide an individualised estimate of intracranial lesion risk following mild traumatic brain injury.
⇒ An estimated 20 000 patients will be included, allowing for robust conclusions and the opportunity to analyse presumed risk factors that are very rare.
⇒ Machine-learning models will be applied to create scores predicting the primary and secondary outcomes.
⇒ Data collectors will not be blinded to outcome data.

## INTRODUCTION

With over 60 million annual cases worldwide,[1] traumatic brain injury (TBI) is one of the most common reasons behind emergency department (ED) visits.[2] The vast majority are mild TBI (mTBI) with an admission Glasgow Coma Scale (GCS) of 13–15,[3] of whom 5%–10% develop an intracranial lesion that might require medical or surgical management.[4 5]

Several decision aids have been developed to identify patients in whom a head CT should be performed. These include the Canadian CT Head Rule (CCHR),[5] New Orleans Criteria (NOC),[6] National Institute of Health and Care Excellence (NICE) guidelines,[7] CT in Head Injury Patients (CHIP) Prediction Rule,[8] the National Emergency X-Radiography Utilisation Study II (NEXUS II) criteria[9] and the Scandinavian Neurotrauma Committee (SNC) guidelines,[10 11] all of which allow for more selective use of CT scanning in patients with mild TBI. The Brain Injury Guidelines (BIG) and the Mild TBI Risk Score have also been developed to help determine which patients are suitable for discharge once the CT has been performed,[12 13] and hence, do not primarily focus on stratifying the risk of lesion detection.

While the above-described algorithms have a high sensitivity for identifying those with intracranial lesions, they share some flaws. To begin, they have low specificity,[14] resulting in CT overuse with unnecessarily high radiation exposure, ED overcrowding and higher costs.[15 16] For example, in a recent prospective, multicentre, external validation of the CHIP Prediction Rule, NOC, CCHR and NICE guidelines, 82% of patients who presented to the ED with a mild TBI underwent a CT scan and 8% had a traumatic intracranial finding. While the sensitivity ranged from 73% to 99%, specificity ranged from only 4% (NOC) to 61% (NICE).[14] These finding were corroborated in another prospective validation of CCHR, NOC and NEXUS II, where 93% of patients underwent CT scanning and specificity ranged from 16% (NOC) to 52% (NEXUS II).[17] Another important limitation is the lack of interaction assessments between risk factors, both in terms of synergism and antagonistic effects, to better estimate intracranial lesion risk. In addition, some novel parameters are not present or detailed specifically in the present guidelines, for example, warfarin versus direct oral anticoagulants or which specific 'neurological deficits' that are high risk. Lastly, the available decision aids do not provide an individualised probability of lesion development. This can be contrasted to the HEART score, which provides risk stratification for major cardiac events in patients with chest-pain,[18] $CHA_2DS_2$-VASc, which gives an annual risk of stroke in those with atrial fibrillation,[19] and Wells score to predict deep vein thrombosis.[20 21]

### Objective

The aim of this study is to create a model that estimates individualised intracranial lesion risks in patients with mTBI who present to the ED.

## METHODS AND ANALYSIS

### Study setting

This will be a retrospective cohort study of adults with mTBI in the ED setting. We will focus on information available to the ED physician when making the decision of whether to perform a head CT scan or not. Thus, the model will incorporate predictors from the patient's history, physical examination and laboratory results. The study will follow the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis guidelines,[22] and has been registered at ClinicalTrials.gov (NCT04995068).

### Study population

The study will include all patients who sought ED care for a mTBI at the Karolinska University Hospital Huddinge, Karolinska University Hospital Solna, Stockholm South General Hospital, Norrtälje Hospital, Danderyd's Hospital and Södertälje Hospital. Together these hospitals serve a catchment area of more than 2 million people in Stockholm, Sweden. All hospitals share the same prehospital TBI management protocol,[23] and adhere to the SNC guidelines for initial

**Table 1** Inclusion and exclusion criteria

| Inclusion criteria | Adult (≥ 15 years)<br>Presented within 24 hours of TBI between 2010 and 2020<br>GCS 13–15 at presentation to the emergency department |
|---|---|
| Exclusion criteria | No CT scan performed<br>Patient from another region in Sweden or another country<br>Penetrating TBI<br>Secondary transfer from other ED<br>Medical record missing<br>Already performed CT scan for other TBI within 30 days |

.ED, emergency department; GCS, Glasgow Coma Scale; TBI, traumatic brain injury.

management of minimal, mild and moderate head injuries.[11] The Karolinska University Hospital Solna, S:t Göran's Hospital and Stockholm South General Hospital also have the capabilities to sample the brain biomarker S100B, thus adhering to the updated SNC guidelines from 2013.[10] Included patients will be adults (≥15 years) with mTBI (GCS 13–15) who presented to the ED within 24 hours of injury between 2010 and 2020 (table 1). Inclusion years will depend on the availability of digital hospital charts, which became centralised during the 2010s throughout the Stockholm Regional Council, but the focus will be on the last 6 years (2015–2020) when data will be available from all hospitals. Patients have been identified by a systemwide search in the electronic medical records software for International Classification of Diseases, Tenth revision (ICD-10) codes for intracranial injury (S06X) and fracture of skull and facial bones (S02X), as well as the ED admissions codes for 'head injury'.

### Data collection

Clinical variables will be retrospectively collected by, or closely supervised by, trained physicians using standardised review protocols. Review will be conducted by members of the direct care team at the different study hospitals. Clinical data will be collected from the health record software TakeCare (CompuGroup Medical Sweden AB, Farsta, Sweden), while imaging data will be collected from the radiological management software Sectra Picture Archiving and Communication System (Sectra AB, Linköping, Sweden). The data will be entered into anonymised case report forms (CRF) (online supplemental additional file 1) in the electronic data capture system REDCap,[24] which can be accessed by the authors AFS and EPT. We will not be able to blind assessors from outcome data.

The primary outcome will be any traumatic lesion on head CT, defined as a cerebral haematoma, subdural haematoma, epidural haematoma, subarachnoid haemorrhage, intraventricular haemorrhage, diffuse axonal injury, depressed skull fracture, traumatic infarction or sinus thrombosis. The secondary outcome will be any clinically significant lesion, defined as a traumatic intracranial finding that led to neurosurgical intervention, hospital admission ≥48 hours due to the TBI or death due

to TBI. We will use the 48-hour cut-off to exclude overnight admissions for minor CT findings that did not result in any further treatment. Due to the retrospective nature of the study, each patient has already been assessed at their index ED visit by a physician who decided the need for a head CT in accordance with the SNC guidelines,[10] and the results of the CT scans have been interpreted by site faculty radiologists (including a board certified radiologist).

Online supplemental additional file 1 details the CRF that will be used to collect inputs for the model. The candidate variables have been chosen due to their previously demonstrated relationship to intracranial lesion risk in the mTBI decision rules CCHR,[5] NOC,[6] NICE guidelines,[7] CHIP Prediction Rule,[8] NEXUS II criteria,[9] SNC guidelines,[10 11] BIG,[12] the Mild TBI Risk score,[13] as well as others which we believe have clinical grounds to be predictive.

## Statistics

An estimated 20 000 patients will be included, which represents all patients treated between 2015 and 2020 who fulfil the inclusion criteria. This means that even in an extreme case of modelling predictors with a total of 100 degrees of freedom, there will still be around 200 patients per predictor parameter. The model will also identify the most important predictors early on, leading to a large sample size for estimating coefficients. A separate statistical analysis plan, together with pilot results, will be published following completion of the first 5000 patients. This will help us to better estimate how many patients are needed to adequately assess the clinical impact of presumed risk factors that are more rare (eg, dual antiplatelet therapy and ventriculoperitoneal shunt).

In order to identify relevant predictors, a regularised regression approach will be attempted. Cross-validation will be used for variable selection. Missing data might be imputed if it is missing at random or completely at random, assuming that the missing rate is within reasonable bounds. We already know that there will be missing S100B values from certain hospitals, and two parallel might will be developed: a 'core' model with variables available at all hospitals, and an additional model with S100B data from the hospitals that use extended laboratory testing. Interaction terms will be used when clinically or statistically motivated. Area under the receiver operating characteristic curve will be used to asses model performance. The dataset will be randomly divided into a derivation and a validation dataset, allowing for internal validation. Overfitting will be avoided by using regularised regression, which will eliminate poorly performing predictors. Furthermore, the validation set will give a non-biased estimate of the final score's performance internally.

## Ethics and dissemination

The study has been approved by the Swedish Ethical Review Authority (Dnr: 2020-05728) who waived the need for informed consent. Each hospital in the Stockholm Region will certify that local regulations are adhered to. The research findings will be disseminated through publications in international, peer-reviewed scientific publications and presentations at conferences.

## Patient and public involvement statement

Patients and members of the public were not involved in the design of this study.

# DISCUSSION
## Potential clinical benefits

While there are several guidelines to help direct patients with mTBI for CT scanning, this will be the first study to provide an individualised estimate of intracranial lesion risk following mTBI, including those with a clinically significant lesion. The large cohort will allow us to analyse presumed risk factors that are very rare, such as intraventricular shunts and haemostatic disorders. In addition, novel parameters that are not present or detailed specifically in the present guidelines will be included, for example, warfarin versus direct oral anticoagulants or which specific 'neurological deficits' that are high risk. Applying a machine-learning algorithm on a large sample size will also allow us to explore the combined effects of predictive or protective factors, both in terms of synergism and antagonistic effects. Together, we believe this will allow us to increase model specificity, without compromising sensitivity, compared with previous decision tools.

## Study limitations

There are some limitations to bear in mind. As all patients do not undergo a CT scan, there will be those with undiagnosed intracranial lesions. In one study, 0.8% of elderly patients with TBI who did not undergo a head CT were diagnosed with intracranial bleeding within 6 weeks, as compared with 0.6% of patients with an initial negative CT scan.[25] This also means that we will only be able to determine SNC guideline compliance with regard to overtriage, but not undertriage, which might impact the characteristics of the study population. Thus, the derived model will not be applicable to patients with mTBI who have not undergone CT scans. However, to mitigate this, the Swedish National Patient Register[26] will be used to detect if any excluded patient was diagnosed with an intracranial lesion within 30 days of their index ED visit. This will also allow us to calculate the incidence of delayed intracranial haemorrhage among the patients with initial normal CT scans. The imperfect reference standard bias, introduced with differential testing depending on the emergency physician CT request, might also inflate the strength of association between predictor variables which are commonly used to determine the need for CT in the SNC guidelines (such as of loss of consciousness or anticoagulation use).[10 11] Lastly, the model will be developed based on patients seeking medical care in Stockholm, Sweden. This means that the generalisability of the data outside of Stockholm can be questioned, and the score will need to undergo prospective validation in other

regions prior to potential clinical implementation. Assessors will also not be blinded to outcome data.

## Trial status

Patient recruitment was commenced on 1 September 2021 and the study is estimated to be completed by 31 December 2023.

**Author affiliations**

¹Department of Neurosurgery, Karolinska University Hospital, Stockholm, Sweden
²Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
³Department of Emergency Medicine, Södersjukhuset, Stockholm, Sweden
⁴Department of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden
⁵Department of Emergency Medicine, Capio S:t Görans Hospital, Stockholm, Sweden
⁶Department of Software and Computer Systems, KTH Royal Institute of Technology, Stockholm, Sweden
⁷Department of Learning and Informatics, Karolinska Institutet, Stockholm, Sweden
⁸Department of Medicine, Karolinska Institutet, Stockholm, Sweden
⁹Department of Emergency Medicine, Danderyds Hospital, Stockholm, Sweden
¹⁰Department of Surgery, Capio S:t Görans Hospital, Stockholm, Sweden
¹¹Department of Clinical Science, Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden
¹²Department of Emergency Medicine, Karolinska University Hospital, Stockholm, Sweden

**Contributors** Study design: AF-S and ET. Draft of manuscript: AF-S. Approval of manuscript: AF-S, CT, LY, EP, MB, PL, SF, IG, VT, RR-W, LS, KW, KÄ, TD, OL, JB and ET. Study supervision: ET.

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**ORCID iDs**
Alexander Fletcher-Sandersjöö http://orcid.org/0000-0002-3558-3045
Philipp Lassarén http://orcid.org/0000-0003-0833-1093
Therese Djärv http://orcid.org/0000-0002-5905-157X
Eric Peter Thelin http://orcid.org/0000-0002-2338-4364

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