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# BMJ Open

## Stockholm score of lesion development on computed tomography following mild traumatic brain injury (SELECT-TBI): study protocol for a multi-centre, population-based, retrospective cohort study

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30 33 **Abstract**

31  
32 34 *Introduction:* Mild traumatic brain injury (mTBI) is one of the most common reasons for  
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34 35 emergency department (ED) visits. A portion of mTBI patients will develop an intracranial  
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36 36 lesion that might require medical or surgical intervention. In these patients, swift diagnosis  
37  
38 37 and management is paramount. Several guidelines have been developed to help direct these  
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40 38 patients for head computed tomography (CT) scanning, but they lack specificity, focus on  
41  
42 39 ruling out lesions, and do not estimate the probability of lesion development. In light of this,  
43  
44 40 the aim of this study is to create a risk stratification score that predicts the probability of  
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46 41 intracranial lesion development in patients with mTBI who present to the ED.  
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50  
51 42 *Methods and analysis:* This will be a retrospective population-based cohort study conducted  
52  
53 43 at all emergency department (ED) hospitals in Stockholm, Sweden. Eligible patients are  
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55 44 adults ( $\geq 15$  years) with mTBI who presented to the ED within 24 hours of injury and  
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57 45 performed a CT scan. The primary outcome will be a traumatic lesion on head CT. The  
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59 46 secondary outcomes will be any clinically significant lesion, defined as an intracranial  
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3 47 finding that led to neurosurgical intervention, discontinuation or reversal of anticoagulant or  
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5 48 antiplatelet medication, hospital admission  $\geq$  48 hours due to the TBI, or death. Machine-  
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7 49 learning models will be applied to create scores predicting the primary and secondary  
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9 50 outcomes. An estimated 20,000 patients will be included.

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13 51 *Ethics and dissemination:* The study has been approved by the Swedish Ethical Review  
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15 52 Authority (Dnr: 2020-05728) and is registered with ClinicalTrials.gov (NCT04995068). The  
16  
17 53 research findings will be disseminated through peer-reviewed scientific publications and  
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19 54 presentations at international conferences.

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21  
22 55 *Trial registration number:* ClinicalTrials.gov (NCT04995068).

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25 56 *Keywords:* traumatic brain injury, mild TBI, head injury, computed tomography  
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## 31 **Article summary**

### 32 *Strengths and limitations of this study*

- 33  
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35 60 ■ This will be the first study to estimate the probability of intracranial lesion development  
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37 61 in mild traumatic brain injury.
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39 62 ■ The population-based study setting means that all patients who sought emergency care  
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41 63 for a mild TBI during the time period will be assessed for eligibility – reducing selection  
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43 64 bias.
- 44  
45 65 ■ An estimated 20,000 patients will be included, allowing for robust conclusions and the  
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47 66 opportunity to analyse presumed risk factors that are very rare.
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49 67 ■ Machine-learning models will be applied to create scores predicting the primary and  
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51 68 secondary outcomes.
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53 69 ■ Data collectors will not be blinded to outcome data.
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## 71 **Introduction**

72 With over 60 million annual cases worldwide [1], traumatic brain injury (TBI) is one of the  
73 most common reasons behind emergency department (ED) visits [2]. The vast majority are  
74 mild (mTBI) with an admission Glasgow Coma Scale (GCS) of 13-15 [3], of whom 5-10 %  
75 will develop an intracranial lesion that might require medical or surgical management [4,5].  
76 Several decision aids have been developed to identify patients in whom a head computed  
77 tomography (CT) should be performed. These include the Canadian CT Head Rule (CCHR)  
78 [5], New Orleans Criteria (NOC) [6], National Institute of Health and Care Excellence  
79 (NICE) guidelines [7], CT in Head Injury Patients (CHIP) Prediction Rule [8], and the  
80 Scandinavian Neurotrauma Committee (SNC) guidelines [9,10]. These commonly provide  
81 algorithms to help clinicians decide on care-pathways and if to perform a CT scan. The Brain  
82 Injury Guidelines (BIG) and the Mild TBI Risk Score have also been developed to help  
83 determine which patients are suitable for discharge once the CT has been performed [11,12],  
84 and hence do not primarily focus on stratifying the risk of lesion development.

85 While the above-described algorithms have a high sensitivity for identifying those with  
86 intracranial lesions, they share two flaws. To begin, they have low specificity [13], resulting  
87 in CT overuse with unnecessarily high radiation exposure, ED overcrowding and higher costs  
88 [14,15]. Secondly, they don't provide a case-by-case probability of lesion development. This  
89 can be contrasted to the HEART score, which provides risk stratification for major cardiac  
90 events in patients with chest-pain [16], CHA<sub>2</sub>DS<sub>2</sub>-VASc, which gives an annual risk of stroke  
91 in those with atrial fibrillation [17], and Wells score to predict deep vein thrombosis [18].  
92 These types of prediction models tailored to a patient's specific features is increasingly  
93 becoming a part of modern-precision "personalized medicine" [19], but have yet to be  
94 implemented in the management of patients presenting with mTBI.

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3 96 *Objective*  
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5 97 The aim of this study is to create a risk stratification score that predicts the probability of  
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7 98 intracranial lesion development in patients with mTBI who present to the ED.  
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13 100 **Methods and analysis**

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15 101 *Study setting*

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17 102 This will be a retrospective cohort study designed to develop a clinical prediction score for  
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19 103 physicians evaluating adults with mTBI in the ED setting. We will focus on information  
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21 104 available to the ED physician when making the decision of whether to perform a head CT  
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23 105 scan or not. Thus, the model will incorporate predictors from the patient's history, physical  
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25 106 examination and laboratory results. The study will follow the transparent reporting of a  
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27 107 multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines  
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29 108 [20], and has been registered at ClinicalTrials.gov (NCT04995068).  
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36 110 *Study population*

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38 111 The goal is to conduct the study at all hospitals with an ED in Stockholm, Sweden  
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40 112 (Karolinska University Hospital Huddinge, Karolinska University Hospital Solna, S:t  
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42 113 Göran's Hospital, Stockholm South General Hospital, Norrtälje Hospital, Danderyd's  
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44 114 Hospital and Södertälje Hospital), which serve a catchment area of more than 2.4 million  
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46 115 people. All hospitals share the same pre-hospital TBI management protocol [21], and adhere  
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48 116 to the SNC guidelines for initial management of minimal, mild and moderate head injuries  
49  
50 117 [10]. Since 2014, the Karolinska University Hospital Solna, S:t Göran's Hospital and  
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52 118 Stockholm South General Hospital have also had the capabilities to sample the brain  
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54 119 biomarker S100B, thus adhering to the updated SNC guidelines from 2013 [9]. Included  
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56 120 patients will be adults ( $\geq 15$  years) with mTBI (GCS 13-15) who presented to the ED within  
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3 121 24 hours of injury between 2010-2020 (Table 1). Inclusion years will depend on the  
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5 122 availability of digital hospital charts, which became centralized during the 2010s throughout  
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7 123 Region Stockholm, but the focus will be on the last six years (2015-2020) when data will be  
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9 124 available from all hospitals. Patients have been identified by a systemwide search in the  
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11 125 electronic medical records software for ICD-10 codes for intracranial injury (S06X) and  
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13 126 fracture of skull and facial bones (S02X), as well as the ED admissions codes for “head  
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15 127 injury”. An estimated 20,000 patients will be included.  
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129 **Table 1: Inclusion and exclusion criteria**

Inclusion criteria	Adult ( $\geq 15$ years) Presented within 24 hours of TBI between 2010-2020 GCS 13-15 at presentation to the emergency department
Exclusion criteria	No CT scan performed Patient from another region in Sweden or another country Penetrating TBI Secondary transfer from other ED Medical record missing

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39 130 Abbreviations: CT = computed tomography; ED = emergency department; GCS = Glasgow  
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41 131 Coma Scale; TBI = traumatic brain injury  
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133 *Data collection*

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48 134 Clinical variables will be retrospectively collected by, or closely supervised by, trained  
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50 135 physicians using standardised review protocols. Review will be conducted by members of the  
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52 136 direct care team in the different hospitals included. Clinical data will be collected from the  
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54 137 health record software TakeCare (CompuGroup Medical Sweden AB, Farsta, Sweden),  
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56 138 Melior (Siemens, Stockholm, Sweden) and Cosmic (Cambio Healthcare Systems, Stockholm,  
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58 139 Sweden), while imaging data will be collected from the radiological management software  
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3 140 Sectra Picture Archiving and Communication System (PACS) (Sectra AB, Linköping,  
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5 141 Sweden). The data will be entered into anonymized case report forms (CRF) (Additional file  
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7 142 1) in the electronic data capture system REDCap [22], which can be accessed by the authors  
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9 143 AFS and EPT. We will not be able to blind assessors from outcome data.

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12 144 The primary outcome will be any traumatic lesion on head CT, defined as a cerebral  
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14 145 haematoma, subdural haematoma, epidural haematoma, subarachnoid haemorrhage,  
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16 146 intraventricular haemorrhage, diffuse axonal injury, skull fracture, traumatic infarction or  
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18 147 sinus thrombosis. The secondary outcome will be any clinically significant lesion, defined as  
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20 148 a traumatic intracranial finding that led to neurosurgical intervention, discontinuation or  
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22 149 reversal of anticoagulant or antiplatelet medication, hospital admission  $\geq 48$  hours due to the  
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24 150 TBI, or death due to TBI. We will use the 48-hour cut-off to exclude overnight admissions  
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26 151 for minor CT findings that did not result in any further treatment. Due to the retrospective  
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28 152 nature of the study, each patient has already been assessed at their index ED visit by a  
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30 153 physician who decided the need for a head CT in accordance with the SNC guidelines [9],  
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32 154 and the results of the CT scans have been interpreted by site faculty radiologists (including a  
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34 155 board certified radiologist).

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36 156 Supplementary file 1 details the CRF that will be used to collect inputs for the model. The  
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38 157 variables have been chosen due to their previously demonstrated relationship to intracranial  
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40 158 lesion development following TBI [5–9,11,12], and their number has been limited to ensure  
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42 159 the practical applicability of the prediction model.

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### 51 52 161 *Statistics*

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54 162 A separate statistical analysis plan, together with pilot results, will be published following  
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56 163 completion of the first 3,000-5,000 patients from the Karolinska University Hospital.

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3 165 *Ethics and dissemination*  
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5 166 The study has been approved by the Swedish Ethical Review Authority (Dnr: 2020-05728)  
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8 167 who waived the need for informed consent. Each hospital in the Stockholm Region will  
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10 168 certify that local regulations are adhered to. The research findings will be disseminated  
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12 169 through publications in international, peer-reviewed scientific publications, and presentations  
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15 170 at conferences.  
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19 172 *Patient and public involvement statement*  
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21 173 As this is a retrospective observational cohort study, patients and the public are not involved  
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23 174 in the design, conduct, or reporting of this study.  
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28 176 **Discussion**  
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30 177 While there are several guidelines to help direct mTBI patients for CT scanning, this will be  
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32 178 the first study to create a score predicting the probability of intracranial lesion development,  
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34 179 including those with a clinically significant lesion. Earlier identification of patients with  
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36 180 lesions requiring treatment may decrease time to intervention [23]. The large cohort will  
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38 181 allow for robust conclusions from the statistical methods, and will also provide us with the  
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40 182 opportunity analyse presumed risk factors that are very rare, such as intraventricular shunts  
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42 183 and haemostatic disorders. Hopefully, we will also be able to increase model specificity  
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44 184 compared to previous decision tools. The population-based study setting also means that all  
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46 185 patients in the Stockholm region who sought emergency care for a mTBI during the time  
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48 186 period will be assessed for eligibility.  
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54 187 There are some limitations to bear in mind. As all patients do not undergo a CT scan, there  
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56 188 will be those with undiagnosed intracranial lesions. In one study, 0.8 % of elderly TBI  
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58 189 patients who did not undergo a head CT were diagnosed with intracranial bleeding within 6  
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3 190 weeks, as compared to 0.6 % of patients with an initial negative CT scan [24]. To minimize  
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5 191 this potential bias, we will scan medical records to make sure that the patient did not return to  
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7 192 the ED within 30 days with a positive CT scan. The imperfect reference standard bias,  
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10 193 introduced with differential testing depending on the emergency physician CT request, might  
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12 194 also inflate the strength of association between predictor variables which are commonly used  
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15 195 to determine the need for CT in the SNC guidelines (such as of loss of consciousness or  
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17 196 anticoagulation use) [9,10]. Assessors will also not be blinded to outcome data.  
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### 198 **Trial status**

199 Patient recruitment was commenced on 2021-09-01 and the study is estimated to be  
200 completed by 2023-12-31.  
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### 202 **Abbreviations**

203	CCHR	Canadian CT Head Rule
204	CHIP	CT in Head Injury Patients
205	CRF	Case report form
206	CT	Computed tomography
207	ED	Emergency department
208	GCS	Glasgow Coma Scale
209	NICE	National Institute of Health and Care Excellence
210	NOC	New Orleans Criteria
211	SNC	Scandinavian Neurotrauma Committee
212	TBI	Traumatic brain injury

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4  
5 215 manuscript: All authors. Study supervision: ET.  
6  
7

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19  
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21  
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24  
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26 223 **Data statement:** Not applicable (study protocol)  
27  
28

29 224 **Word count:** 1,400  
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#### 34 226 **Additional material**

35  
36 227 File name: Additional file 1  
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38 228 File format: pdf  
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40 229 Title: Case report form  
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43 230 Description: Case report form that will be used for data collection  
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STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

## SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section	Item No	Description	Location
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 3
	2b	All items from the World Health Organization Trial Registration Data Set	p. 3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	p. 9
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	N/A
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
<b>Introduction</b>			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	p. 3-4
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	p. 4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	p. 5-7
<b>Methods: Participants, interventions, and outcomes</b>			



1		9	Description of study settings (eg, community clinic, academic hospital)	
2	Study setting		and list of countries where data will be collected. Reference to where list	p. 5-7
3			of study sites can be obtained	
4				
5	Eligibility	10	Inclusion and exclusion criteria for participants. If applicable, eligibility	
6	criteria		criteria for study centres and individuals who will perform the	p. 6
7			interventions (eg, surgeons, psychotherapists)	
8				
9		11a	Interventions for each group with sufficient detail to allow replication,	
10			including how and when they will be administered	N/A
11				
12		11b	Criteria for discontinuing or modifying allocated interventions for a given	
13			trial participant (eg, drug dose change in response to harms, participant	N/A
14			request, or improving/worsening disease)	
15	Interventions			
16		11c	Strategies to improve adherence to intervention protocols, and any	
17			procedures for monitoring adherence (eg, drug tablet return, laboratory	N/A
18			tests)	
19				
20		11d	Relevant concomitant care and interventions that are permitted or	
21			prohibited during the trial	N/A
22				
23				
24		12	Primary, secondary, and other outcomes, including the specific	
25			measurement variable (eg, systolic blood pressure), analysis metric (eg,	
26	Outcomes		change from baseline, final value, time to event), method of aggregation	p. 6-7
27			(eg, median, proportion), and time point for each outcome. Explanation	
28			of the clinical relevance of chosen efficacy and harm outcomes is	
29			strongly recommended	
30				
31				
32				
33	Participant	13	Time schedule of enrolment, interventions (including any run-ins and	
34	timeline		washouts), assessments, and visits for participants. A schematic	p. 8
35			diagram is highly recommended (see Figure)	
36				
37		14	Estimated number of participants needed to achieve study objectives	
38	Sample size		and how it was determined, including clinical and statistical assumptions	p. 6
39			supporting any sample size calculations	
40				
41				
42	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target	
43			sample size	p. 6
44				
45	<b>Methods: Assignment of interventions (for controlled trials)</b>			
46				
47	Allocation:			
48				
49		16a	Method of generating the allocation sequence (eg, computer-generated	
50	Sequence		random numbers), and list of any factors for stratification. To reduce	
51	generation		predictability of a random sequence, details of any planned restriction	N/A
52			(eg, blocking) should be provided in a separate document that is	
53			unavailable to those who enrol participants or assign interventions	
54				
55				
56	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central	
57	concealme		telephone; sequentially numbered, opaque, sealed envelopes),	
58	nt		describing any steps to conceal the sequence until interventions are	N/A
59	mechanis		assigned	
60	m			

1	Implement	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
2	ation			
3				
4	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
5	(masking)			
6				
7		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
8				
9				
10				
11	<b>Methods: Data collection, management, and analysis</b>			
12				
13		18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	p. 7
14	Data			
15	collection			
16	methods			
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21		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
22				
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24				
25				
26		19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	p. 6-7
27	Data			
28	management			
29				
30				
31				
32	Statistical	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	p. 7
33	methods			
34				
35				
36		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
37				
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39				
40		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
41				
42				
43				
44	<b>Methods: Monitoring</b>			
45				
46		21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
47	Data			
48	monitoring			
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53		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	p. 7
54				
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56				
57		22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
58	Harms			
59				
60				

1	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
2				
3				
4	<b>Ethics and dissemination</b>			
5				
6	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 7
7				
8				
9				
10				
11	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	N/A
12				
13				
14				
15				
16	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	N/A
17				
18				
19				
20		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
21				
22				
23	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 6
24				
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27	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 9
28				
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31	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 6
32				
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35	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
36				
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38				
39	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 7
40				
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44		31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
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48		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
49				
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51	<b>Appendices</b>			
52				
53	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
54				
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56				
57	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
58				
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1 \*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &  
2 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and  
3 dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-  
4 NonCommercial-NoDerivs 3.0 Unported](#)" license.  
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For peer review only

# Variable list

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Patient ID

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Hospital

- Danderyds Sjukhus  
 Karolinska Universitetssjukhuset Solna  
 Karolinska Universitetssjukhuset Huddinge  
 Norrtälje Sjukhus  
 S:t Görans Sjukhus  
 Södertälje Sjukhus  
 Södersjukhuset  
 (Hospital where the emergency department was located)

Sex

- Male    Female

Age

\_\_\_\_\_

(Years)

Date of trauma

\_\_\_\_\_

(YYYY-MM-DD (if unknown, leave blank))

Time of trauma

\_\_\_\_\_

(HH:MM (if unknown, leave blank))

Emergency department admission date

\_\_\_\_\_

(YYYY-MM-DD (if unknown, leave blank))

Emergency department admission time

\_\_\_\_\_

(HH:MM (if unknown, leave blank))

Time from injury to emergency department admission

- 0-3 hours  
 3-6 hours  
 6-12 hours  
 12-24 hours  
 Unknow

Doctor assessment date

\_\_\_\_\_

(YYYY-MM-DD (if unknown, leave blank))

Doctor assessment time

\_\_\_\_\_

(HH:MM (if unknown, leave blank))

Date of discharge from emergency room

\_\_\_\_\_

(YYYY-MM-DD (if unknown, leave blank))

1 Time of discharge from emergency room

2  
3 (HH:MM (if unknown, leave blank))

4  
5 Comorbidities

- 6  
7  None of the below
- 8  Dementia
- 9  Alcoholism
- 10  Liver cirrhosis
- 11  Chronic renal impairment
- 12  Intraventricular shunt
- 13  Anticoagulation treatment
- 14  Antiplatelet treatment
- 15  Bleeding disorder  
(Select all that apply)

16 If "anticoagulation treatment" = yes, specify type(s)

- 17  Warfarin
- 18  Apixaban (Eliquis)
- 19  Rivaroxaban (Xarelto)
- 20  Dabigatran (Pradaxa)
- 21  Edoxaban (Lixiana)
- 22  LMWH (low-molecular-weight heparin)
- 23  Other  
(Select all that apply)

24  
25 If "antiplatelet treatment" = yes, specify type(s)

- 26  ASA (Trombyl)
- 27  Clopidogrel (Plavix)
- 28  Ticagrelor (Brilique)
- 29  Prasugrel (Effient)
- 30  Dipyridamole (Persantin)
- 31  Ticlopidine (Ticlid)
- 32  Eptifibatide (Integrilin)
- 33  Other  
(Select all that apply)

34  
35 If "bleeding disorder" = yes, specify type

36 \_\_\_\_\_

37  
38 Trauma mechanism

- 39  Low energy fall (same level)
- 40  High energy fall (> 1 meter or > 5 steps)
- 41  Motor vehicle accident (not motorcycle)
- 42  Motorcycle accident
- 43  Bicycle accident
- 44  Pedestrian hit by traffic
- 45  Other traffic accident
- 46  Shot by gun
- 47  Stabbed by sharp object
- 48  Struck by blunt object
- 49  Blast injury (e.g. explosion)
- 50  Other
- 51  Unknown

52 Multitrauma

- 53  Yes  No
- 54 (Defined as radiology ordered for body part other
- 55 than brain / cervical spine due to suspicion of
- 56 traumatic injury)
- 57
- 58
- 59
- 60

1 2 3 4 5 6 7	If "multitrauma" = yes, specify	<input type="checkbox"/> Thorax <input type="checkbox"/> Abdomen <input type="checkbox"/> Spine (thoracic or lumbar) <input type="checkbox"/> Upper Extremity <input type="checkbox"/> Lower Extremity (Select all that apply)
8 9 10 11	GCS = 15 before injury	<input type="radio"/> Yes <input type="radio"/> No ("No" means that the patient was GCS 14 or below prior to injury (e.g. dementia))
12 13 14 15 16 17	GCS on emergency department admission	<input type="radio"/> GCS = 15 <input type="radio"/> GCS = 14 <input type="radio"/> GCS = 13 (GCS when the physician performed the first assessment of the patient)
18 19 20 21 22	GCS eye score	<input type="radio"/> 4 (eyes open spontaneously) <input type="radio"/> 3 (eyes open to verbal command) <input type="radio"/> 2 (eyes open to pain) <input type="radio"/> Unknown
23 24 25 26 27	GCS verbal score	<input type="radio"/> 5 (orientated to time, person, place) <input type="radio"/> 4 (confused) <input type="radio"/> 3 (inappropriate words) <input type="radio"/> Unknown
28 29 30 31 32 33	GCS motor score	<input type="radio"/> 6 (obeys command) <input type="radio"/> 5 (moves to localised pain) <input type="radio"/> 4 (flex to withdraw from pain) <input type="radio"/> Unknown
34 35 36 37	Deterioration in GCS after first assessment	<input type="radio"/> Yes <input type="radio"/> No (Deteriorated in GCS after initial assessment of GCS)
38 39 40 41	Intoxicated	<input type="radio"/> Yes <input type="radio"/> No (Intoxicated on assessment (e.g. alcohol))
42 43 44 45 46 47 48 49 50	If "intoxicated" = yes, specify substance(s)	<input type="checkbox"/> Alcohol <input type="checkbox"/> Central stimulants (e.g. amphetamines, cocaine, LSD, ecstasy) <input type="checkbox"/> Anxiolytics (e.g. benzodiazepines) <input type="checkbox"/> Cannabis <input type="checkbox"/> Opioids <input type="checkbox"/> Other <input type="checkbox"/> Unknown (Select all that apply)
51 52 53 54 55	Pupillary status	<input type="radio"/> Normal <input type="radio"/> Unilateral dilation <input type="radio"/> Bilateral dilation (If not detailed, choose "normal")
56 57 58 59 60	If abnormal pupillary status - reactive to light?	<input type="radio"/> Yes <input type="radio"/> No

16 Post-traumatic neurological deficit  None of the below  
 2  Weakness in extremity  
 3  Numbness in extremity  
 4  Diplopia (double-vision)  
 5  Blurry vision  
 6  Dysphasia (problems with speech)  
 7  Dizziness / loss of balance  
 8  Loss of coordination  
 9  Other  
 10 (Select all that apply. Do NOT check if patient  
 11 had impairment prior to injury (e.g. already  
 12 paralyzed patient))

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14 If "other deficit" = yes, specify \_\_\_\_\_

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17 Other worrisky factors  None of the below  
 18  Amnesia  
 19  Confirmed loss of consciousness  
 20  Suspected loss of consciousness (e.g. if patient  
 21 is unsure)  
 22  Vomiting  
 23  Persistent headache  
 24  Seizure  
 25  Scalp wound that needed suturing (excl. face)  
 26  Suspected open or depressed skull fracture  
 27  Sign(s) of skull base fracture  
 28 (Select all that apply)

---

30 If "amnesia" = yes, specify type(s)  Retrograde (can't recall entire traumatic event)  
 31  Anterograde (can't remember new information)  
 32  Combined retrograde and anterograde  
 33  Unknown / missing

---

35 If "loss of consciousness" = yes, specify if it was  Yes  
 36 due to the head injury (i.e. not syncope / fainting)  No  
 37  Unclear

---

39 If "vomiting" = yes, specify amount  Once  
 40  More than once  
 41  Unknown / missing

---

44 If "sign(s) of skull base fracture" = yes, specify  Racoon-eyes (bruising around eye - "black eye",  
 45 "brillenhematoma")  
 46  Battle's sign (bruising of the mastoid process  
 47 behind ear)  
 48  Rhinorrhea (CSF-leak from nose)  
 49  Otorrhea (CSF-leak from ear)  
 50  Anosmia (loss of smell)  
 51  Hematotympanon (blood behind ear drum)  
 52  Deafness  
 53  Nystagmus  
 54  Fascial nerve paralysis  
 55  Other

---

56 If "other sign(s) of skull base fracture" = yes,  
 57 specify \_\_\_\_\_

---

60 Lab sampled  Yes  No



1	Date of lab sampling (first test)	
2		
3		_____
4		(YYYY-MM-DD)
5	Time of lab sampling (first test)	
6		
7		_____
8		(HH:MM)
9		
10	S100B	
11		
12		_____
13		(µg/L)
14	PK(INR)	
15		_____
16		
17	APT-time	
18		
19		_____
20		(seconds)
21		
22	Hemoglobin (Hb)	
23		
24		_____
25		(g/L)
26	Platelet count	
27		
28		_____
29		(150 x 10 <sup>9</sup> /L)
30	Serum ethanol	
31		
32		_____
33		(mmol/L)
34	Alcohol promille level (breathalyzer)	
35		
36		_____
37		(promille)
38		
39	Date of CT scan	
40		
41		_____
42		(YYYY-MM-DD)
43	Time of CT scan	
44		
45		_____
46		(HH:MM)
47		
48	Intracranial lesion on CT	<input type="radio"/> Yes <input type="radio"/> No
49	If "intracranial lesion on CT" = yes, specify type(s)	
50		<input type="checkbox"/> Cerebral contusion
51		<input type="checkbox"/> Traumatic subarachnoid haemorrhage
52		<input type="checkbox"/> Epidural hematoma
53		<input type="checkbox"/> Acute subdural hematoma
54		<input type="checkbox"/> Chronic subdural hematoma
55		<input type="checkbox"/> Intraventricular hematoma
56		<input type="checkbox"/> Diffuse axonal injury
57		<input type="checkbox"/> Sinus thrombosis
58		<input type="checkbox"/> Traumatic infarct
59		<input type="checkbox"/> Skull fracture (neurocranium, not face)
60		(Select all that apply)

1 If "skull fracture" = yes, specify type(s)

- 2  Linear fracture with impression  
 3  Linear fracture without impression  
 4  Crush fracture with impression  
 5  Crush fracture without impression  
 6  Other

7 If "intracranial lesion on CT" = yes, specify  
 8 management

- 9  None (sent home from emergency department)  
 10  Admission < 48 hours due to TBI ("overnight  
 11 observation")  
 12  Admission > 48 hours due to TBI  
 13  Paus or reversal of anticoagulants or antiplatelets  
 14  Intubated due to TBI  
 15  Transfer to neurosurgical department  
 16  Death due to TBI  
 (Select all that apply)

17 If patient was admitted due to TBI, specify amount of  
 18 days in hospital

\_\_\_\_\_

19  
 20 Follow-up CT performed

- 21  Yes  No

22  
 23 If "follow-up CT performed" = yes, specify reason(s)

- 24  Decided on admission regardless of neurology  
 25  Decreased consciousness  
 26  Increased headache  
 27  New neurological abnormality  
 28  Vomiting  
 29  Other  
 30  Unclear / unknown

31 If "follow-up CT performed" = yes, specify if the  
 32 lesion progressed

- 33  Yes  No

34 Re-admission within 30 days with CT-verified  
 35 intracranial lesion

- 36  Yes  No  
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# BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-060679.R1
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3 1 Stockholm score of lesion detection on computed tomography  
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6 2 following mild traumatic brain injury (SELECT-TBI): study protocol  
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9 3 for a multi-centre, retrospective, observational cohort study  
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29 33 **Abstract**

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32 34 *Introduction:* Mild traumatic brain injury (mTBI) is one of the most common reasons for  
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34 35 emergency department (ED) visits. A portion of mTBI patients will develop an intracranial  
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36 36 lesion that might require medical or surgical intervention. In these patients, swift diagnosis  
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38 37 and management is paramount. Several guidelines have been developed to help direct mTBI  
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40 38 patients for head computed tomography (CT) scanning, but they lack specificity, do not  
41  
42 39 consider the interactions between risk factors, and do not provide an individualised estimate  
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44 40 of intracranial lesion risk. The aim of this study is to create a model that estimates  
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46 41 individualised intracranial lesion risks in patients with mTBI who present to the ED.  
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51 42 *Methods and analysis:* This will be a retrospective cohort study conducted at emergency  
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53 43 department (ED) hospitals in Stockholm, Sweden. Eligible patients are adults ( $\geq 15$  years)  
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55 44 with mTBI who presented to the ED within 24 hours of injury and performed a CT scan. The  
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57 45 primary outcome will be a traumatic lesion on head CT. The secondary outcomes will be any  
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59 46 clinically significant lesion, defined as an intracranial finding that led to neurosurgical  
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3 71 mild (mTBI) with an admission Glasgow Coma Scale (GCS) of 13-15 [3], of whom 5-10 %  
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5 72 develop an intracranial lesion that might require medical or surgical management [4,5].  
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8 73 Several decision aids have been developed to identify patients in whom a head computed  
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10 74 tomography (CT) should be performed. These include the Canadian CT Head Rule (CCHR)  
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12 75 [5], New Orleans Criteria (NOC) [6], National Institute of Health and Care Excellence  
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14 76 (NICE) guidelines [7], CT in Head Injury Patients (CHIP) Prediction Rule [8], the National  
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16 77 Emergency X-Radiography Utilization Study II (NEXUS II) criteria [9], and the  
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18 78 Scandinavian Neurotrauma Committee (SNC) guidelines [10,11], all of which allow for more  
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20 79 selective use of CT scanning in patients with mild TBI. The Brain Injury Guidelines (BIG)  
21  
22 80 and the Mild TBI Risk Score have also been developed to help determine which patients are  
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24 81 suitable for discharge once the CT has been performed [12,13], and hence do not primarily  
25  
26 82 focus on stratifying the risk of lesion detection.  
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31 83 While the above-described algorithms have a high sensitivity for identifying those with  
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33 84 intracranial lesions, they share some flaws. To begin, they have low specificity [14], resulting  
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35 85 in CT overuse with unnecessarily high radiation exposure, ED overcrowding and higher costs  
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37 86 [15,16]. For example, in a recent prospective, multicentre, external validation of the CHIP  
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39 87 Prediction Rule, NOC, CCHR, and NICE guidelines, 82% of patients who presented to the  
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41 88 ED with a mild TBI underwent a CT scan and 8% had a traumatic intracranial finding. While  
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43 89 the sensitivity ranged from 73% to 99%, specificity ranged from only 4% (NOC) to 61%  
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45 90 (NICE) [17]. These findings were corroborated in another prospective validation of CCHR,  
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47 91 NOC and NEXUS II, where 93% of patients underwent CT scanning and specificity ranged  
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49 92 from 16% (NOC) to 52% (NEXUS II) [18]. Another important limitation is the lack of  
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51 93 interaction assessments between risk factors, both in terms of synergism and antagonistic  
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53 94 effects, to better estimate intracranial lesion risk. In addition, some novel parameters are not  
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55 95 present or detailed specifically in the present guidelines, for example warfarin vs direct oral  
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3 96 anticoagulants or which specific “neurological deficits” that are high risk. Lastly, the  
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5 97 available decision aids don’t provide an individualised probability of lesion development.  
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8 98 This can be contrasted to the HEART score, which provides risk stratification for major  
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10 99 cardiac events in patients with chest-pain [19], CHA<sub>2</sub>DS<sub>2</sub>-VASc, which gives an annual risk  
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12 100 of stroke in those with atrial fibrillation [20], and Wells score to predict deep vein thrombosis  
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15 101 [21]. [22]

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### 103 *Objective*

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

106

## 107 **Methods and analysis**

### 108 *Study setting*

109 This will be a retrospective cohort study of adults with mTBI in the ED setting. We will  
110 focus on information available to the ED physician when making the decision of whether to  
111 perform a head CT scan or not. Thus, the model will incorporate predictors from the patient’s  
112 history, physical examination and laboratory results. The study will follow the transparent  
113 reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD)  
114 guidelines [23], and has been registered at ClinicalTrials.gov (NCT04995068).

115

### 116 *Study population*

117 The study will include all patients who sought ED care for a mTBI at the Karolinska  
118 University Hospital Huddinge, Karolinska University Hospital Solna, Stockholm South  
119 General Hospital, Norrtälje Hospital, Danderyd’s Hospital and Södertälje Hospital. Together  
120 these hospitals serve a catchment area of more than 2 million people in Stockholm, Sweden.

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3 121 All hospitals share the same pre-hospital TBI management protocol [24], and adhere to the  
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5 122 SNC guidelines for initial management of minimal, mild and moderate head injuries [11].  
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8 123 The Karolinska University Hospital Solna, S:t Göran's Hospital and Stockholm South  
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10 124 General Hospital also have the capabilities to sample the brain biomarker S100B, thus  
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12 125 adhering to the updated SNC guidelines from 2013 [10]. Included patients will be adults ( $\geq$   
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14 126 15 years) with mTBI (GCS 13-15) who presented to the ED within 24 hours of injury  
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16 127 between 2010-2020 (Table 1). Inclusion years will depend on the availability of digital  
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18 128 hospital charts, which became centralized during the 2010s throughout the Stockholm  
19  
20 129 Regional Council, but the focus will be on the last six years (2015-2020) when data will be  
21  
22 130 available from all hospitals. Patients have been identified by a systemwide search in the  
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24 131 electronic medical records software for ICD-10 codes for intracranial injury (S06X) and  
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26 132 fracture of skull and facial bones (S02X), as well as the ED admissions codes for "head  
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28 133 injury".  
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135 **Table 1: Inclusion and exclusion criteria**

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

136 Abbreviations: CT = computed tomography; ED = emergency department; GCS = Glasgow

137 Coma Scale; TBI = traumatic brain injury

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3 139 *Data collection*  
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5 140 Clinical variables will be retrospectively collected by, or closely supervised by, trained  
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7 141 physicians using standardised review protocols. Review will be conducted by members of the  
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9 142 direct care team at the different study hospitals. Clinical data will be collected from the health  
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11 143 record software TakeCare (CompuGroup Medical Sweden AB, Farsta, Sweden), while  
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13 144 imaging data will be collected from the radiological management software Sectra Picture  
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15 145 Archiving and Communication System (PACS) (Sectra AB, Linköping, Sweden). The data  
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17 146 will be entered into anonymized case report forms (CRF) (Additional file 1) in the electronic  
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19 147 data capture system REDCap [25], which can be accessed by the authors AFS and EPT. We  
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21 148 will not be able to blind assessors from outcome data.  
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26 149 The primary outcome will be any traumatic lesion on head CT, defined as a cerebral  
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28 150 haematoma, subdural haematoma, epidural haematoma, subarachnoid haemorrhage,  
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30 151 intraventricular haemorrhage, diffuse axonal injury, depressed skull fracture, traumatic  
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32 152 infarction or sinus thrombosis. The secondary outcome will be any clinically significant  
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34 153 lesion, defined as a traumatic intracranial finding that led to neurosurgical intervention,  
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36 154 hospital admission  $\geq$  48 hours due to the TBI, or death due to TBI. We will use the 48-hour  
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38 155 cut-off to exclude overnight admissions for minor CT findings that did not result in any  
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40 156 further treatment. Due to the retrospective nature of the study, each patient has already been  
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42 157 assessed at their index ED visit by a physician who decided the need for a head CT in  
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44 158 accordance with the SNC guidelines [10], and the results of the CT scans have been  
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46 159 interpreted by site faculty radiologists (including a board certified radiologist).  
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52 160 Additional file 1 details the CRF that will be used to collect inputs for the model. The  
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54 161 candidate variables have been chosen due to their previously demonstrated relationship to  
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56 162 intracranial lesion risk in the mTBI decision rules CCHR [5], NOC [6], NICE guidelines [7],  
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58 163 CHIP Prediction Rule [8], NEXUS II criteria [9], SNC guidelines [10,11], BIG [12], the Mild  
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3 164 TBI Risk score [13], as well as others which we believe have clinical grounds to be  
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5 165 predictive.

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10 167 *Statistics*

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13 168 An estimated 20,000 patients will be included, which represents all patients treated between  
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15 169 2015 – 2020 who fulfil the inclusion criteria. This means that even in an extreme case of  
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17 170 modelling predictors with a total of 100 degrees of freedom, there will still be around 200  
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19 171 patients per predictor parameter. The model will also identify the most important predictors  
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21 172 early on, leading to a large sample size for estimating coefficients. A separate statistical  
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23 173 analysis plan, together with pilot results, will be published following completion of the first  
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25 174 5,000 patients. This will help us to better estimate how many patients are needed to  
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27 175 adequately assess the clinical impact of presumed risk factors that are more rare (for example  
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29 176 dual antiplatelet therapy and ventriculoperitoneal shunt).

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34 177 In order to identify relevant predictors, a regularized regression approach will be attempted.

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36 178 Cross validation will be used for variable selection. Missing data might be imputed if it is  
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38 179 missing at random or completely at random, assuming that the missing rate is within

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40 180 reasonable bounds. We already know that there will be missing S100B values from certain

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42 181 hospitals, and two parallel models will be developed: a “core” model with variables available

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44 182 at all hospitals, and an additional model with S100B data from the hospitals that use extended

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46 183 laboratory testing. Interaction terms will be used when clinically or statistically motivated.

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48 184 Area under the receiver operating characteristic curve (AUC) will be used to assess model

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50 185 performance. The dataset will be randomly divided into a derivation- and a validation dataset,

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52 186 allowing for internal validation. Overfitting will be avoided by using regularized regression,

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54 187 which will eliminate poorly performing predictors. Furthermore, the validation set will give a

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56 188 non-biased estimate of the final score’s performance internally.  
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5 190 *Ethics and dissemination*6  
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8 191 The study has been approved by the Swedish Ethical Review Authority (Dnr: 2020-05728)9  
10 192 who waived the need for informed consent. Each hospital in the Stockholm Region will11  
12 193 certify that local regulations are adhered to. The research findings will be disseminated13  
14 194 through publications in international, peer-reviewed scientific publications, and presentations15  
16 195 at conferences.  
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21 197 *Patient and public involvement statement*22  
23 198 Patients and members of the public were not involved in the design of this study.24  
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26 19927  
28 200 **Discussion**29  
30 201 *Potential clinical benefits*31  
32 202 While there are several guidelines to help direct mTBI patients for CT scanning, this will be33  
34 203 the first study to provide an individualised estimate of intracranial lesion risk following mild35  
36 204 traumatic brain injury, including those with a clinically significant lesion. The large cohort37  
38 205 will allow us to analyse presumed risk factors that are very rare, such as intraventricular39  
40 206 shunts and haemostatic disorders. In addition, novel parameters that are not present or41  
42 207 detailed specifically in the present guidelines will be included, for example warfarin vs direct43  
44 208 oral anticoagulants or which specific “neurological deficits” that are high risk. Applying a45  
46 209 machine-learning algorithm on a large sample size will also allow us to explore the combined47  
48 210 effects of predictive or protective factors, both in terms of synergism and antagonistic effects.49  
50 211 Together, we believe this will allow us to increase model specificity, without compromising51  
52 212 sensitivity, compared to previous decision tools.  
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3 214 *Study limitations*  
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5 215 There are some limitations to bear in mind. As all patients do not undergo a CT scan, there  
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7 216 will be those with undiagnosed intracranial lesions. In one study, 0.8 % of elderly TBI  
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9 217 patients who did not undergo a head CT were diagnosed with intracranial bleeding within 6  
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11 218 weeks, as compared to 0.6 % of patients with an initial negative CT scan [26]. This also  
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13 219 means that we will only be able to determine SNC-guideline compliance with regards to  
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15 220 overtriage, but not undertriage, which might impact the characteristics of the study  
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17 221 population. Thus, the derived model will not be applicable to mTBI patients who have not  
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19 222 undergone CT scans. However, to mitigate this, the Swedish National Patient Register [27]  
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21 223 will be used to detect if any excluded patient was diagnosed with an intracranial lesion within  
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23 224 30 days of their index ED visit. This will also allow us to calculate the incidence of delayed  
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25 225 intracranial haemorrhage among the patients with initial normal CT scans. The imperfect  
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27 226 reference standard bias, introduced with differential testing depending on the emergency  
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29 227 physician CT request, might also inflate the strength of association between predictor  
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31 228 variables which are commonly used to determine the need for CT in the SNC guidelines  
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33 229 (such as of loss of consciousness or anticoagulation use) [10,11]. Lastly, the model will be  
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35 230 developed based on patients seeking medical care in Stockholm, Sweden. This means that the  
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37 231 generalisability of the data outside of Stockholm can be questioned, and the score will need  
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39 232 to undergo prospective validation in other regions prior to potential clinical implementation.  
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41 233 Assessors will also not be blinded to outcome data.  
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51 235 **Trial status**  
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53 236 Patient recruitment was commenced on 2021-09-01 and the study is estimated to be  
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55 237 completed by 2023-12-31.  
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3 239 **Abbreviations**  
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5 240 AUC Area under the receiver operating characteristic curve  
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7 241 CCHR Canadian CT Head Rule  
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9 242 CHIP CT in Head Injury Patients  
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11 243 CRF Case report form  
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13 244 CT Computed tomography  
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15 245 ED Emergency department  
16  
17 246 GCS Glasgow Coma Scale  
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19 247 NEXUS II National Emergency X-Radiography Utilization Study II  
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21 248 NICE National Institute of Health and Care Excellence  
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23 249 NOC New Orleans Criteria  
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25 250 SNC Scandinavian Neurotrauma Committee  
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27 251 TBI Traumatic brain injury  
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36 253 **Author contributions:** Study design: AFS, ET. Draft of manuscript: AFS. Approval of  
37  
38 254 manuscript: AFS, CT, LY, EP, MB, PL, SF, IG, VT, RRW, LS, KW, KÄ, TD, OL, JB, ET.  
39  
40 255 Study supervision: ET.  
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43

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60

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264 **Word count:** 1,400

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266 **Additional material**

267 File name: Additional file 1

268 File format: pdf

269 Title: Case report form

270 Description: Case report form used for data collection

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# Variable list

1  
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5 Patient ID  
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8 Hospital

- 9  Danderyds Sjukhus  
10  Karolinska Universitetssjukhuset Solna  
11  Karolinska Universitetssjukhuset Huddinge  
12  Norrtälje Sjukhus  
13  S:t Görans Sjukhus  
14  Södertälje Sjukhus  
15  Södersjukhuset  
16 (Hospital where the emergency department was  
17 located)
- 

18 Sex

- 19  Male  Female
- 

20 Age

21 \_\_\_\_\_  
22 (Years)  
23

---

24 Date of trauma

25 \_\_\_\_\_  
26 (YYYY-MM-DD (if unknown, leave blank))  
27

---

28 Time of trauma

29 \_\_\_\_\_  
30 (HH:MM (if unknown, leave blank))  
31

---

32 Emergency department admission date

33 \_\_\_\_\_  
34 (YYYY-MM-DD (if unknown, leave blank))  
35

---

36 Emergency department admission time

37 \_\_\_\_\_  
38 (HH:MM (if unknown, leave blank))  
39

---

40 Time from injury to emergency department admission

- 41  0-3 hours  
42  3-6 hours  
43  6-12 hours  
44  12-24 hours  
45  Unknow  
46
- 

47 Doctor assessment date

48 \_\_\_\_\_  
49 (YYYY-MM-DD (if unknown, leave blank))  
50

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51 Doctor assessment time

52 \_\_\_\_\_  
53 (HH:MM (if unknown, leave blank))  
54

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55 Date of discharge from emergency room

56 \_\_\_\_\_  
57 (YYYY-MM-DD (if unknown, leave blank))  
58  
59  
60

1 Time of discharge from emergency room

2  
3 (HH:MM (if unknown, leave blank))

4  
5 Comorbidities

- 6  
7  None of the below  
8  Dementia  
9  Alcoholism  
10  Liver cirrhosis  
11  Chronic renal impairment  
12  Intraventricular shunt  
13  Anticoagulation treatment  
14  Antiplatelet treatment  
15  Bleeding disorder  
(Select all that apply)

16 If "anticoagulation treatment" = yes, specify type(s)

- 17  Warfarin  
18  Apixaban (Eliquis)  
19  Rivaroxaban (Xarelto)  
20  Dabigatran (Pradaxa)  
21  Edoxaban (Lixiana)  
22  LMWH (low-molecular-weight heparin)  
23  Other  
(Select all that apply)

24  
25 If "antiplatelet treatment" = yes, specify type(s)

- 26  ASA (Tromblyl)  
27  Clopidogrel (Plavix)  
28  Ticagrelor (Brilique)  
29  Prasugrel (Effient)  
30  Dipyridamole (Persantin)  
31  Ticlopidine (Ticlid)  
32  Eptifibatide (Integrilin)  
33  Other  
(Select all that apply)

34  
35 If "bleeding disorder" = yes, specify type

36  
37  
38 Trauma mechanism

- 39  Low energy fall (same level)  
40  High energy fall (> 1 meter or > 5 steps)  
41  Motor vehicle accident (not motorcycle)  
42  Motorcycle accident  
43  Bicycle accident  
44  Pedestrian hit by traffic  
45  Other traffic accident  
46  Shot by gun  
47  Stabbed by sharp object  
48  Struck by blunt object  
49  Blast injury (e.g. explosion)  
50  Other  
51  Unknown

52 Multitrauma

- 53  Yes  No  
54 (Defined as radiology ordered for body part other  
55 than brain / cervical spine due to suspicion of  
56 traumatic injury)  
57  
58  
59  
60

1 2 3 4 5 6 7	If "multitrauma" = yes, specify	<input type="checkbox"/> Thorax <input type="checkbox"/> Abdomen <input type="checkbox"/> Spine (thoracic or lumbar) <input type="checkbox"/> Upper Extremity <input type="checkbox"/> Lower Extremity (Select all that apply)
8 9 10 11	GCS = 15 before injury	<input type="radio"/> Yes <input type="radio"/> No ("No" means that the patient was GCS 14 or below prior to injury (e.g. dementia))
12 13 14 15 16 17	GCS on emergency department admission	<input type="radio"/> GCS = 15 <input type="radio"/> GCS = 14 <input type="radio"/> GCS = 13 (GCS when the physician performed the first assessment of the patient)
18 19 20 21 22	GCS eye score	<input type="radio"/> 4 (eyes open spontaneously) <input type="radio"/> 3 (eyes open to verbal command) <input type="radio"/> 2 (eyes open to pain) <input type="radio"/> Unknown
23 24 25 26 27	GCS verbal score	<input type="radio"/> 5 (orientated to time, person, place) <input type="radio"/> 4 (confused) <input type="radio"/> 3 (inappropriate words) <input type="radio"/> Unknown
28 29 30 31 32 33	GCS motor score	<input type="radio"/> 6 (obeys command) <input type="radio"/> 5 (moves to localised pain) <input type="radio"/> 4 (flex to withdraw from pain) <input type="radio"/> Unknown
34 35 36 37	Deterioration in GCS after first assessment	<input type="radio"/> Yes <input type="radio"/> No (Deteriorated in GCS after initial assessment of GCS)
38 39 40 41	Intoxicated	<input type="radio"/> Yes <input type="radio"/> No (Intoxicated on assessment (e.g. alcohol))
42 43 44 45 46 47 48 49 50	If "intoxicated" = yes, specify substance(s)	<input type="checkbox"/> Alcohol <input type="checkbox"/> Central stimulants (e.g. amphetamines, cocaine, LSD, ecstasy) <input type="checkbox"/> Anxiolytics (e.g. benzodiazepines) <input type="checkbox"/> Cannabis <input type="checkbox"/> Opioids <input type="checkbox"/> Other <input type="checkbox"/> Unknown (Select all that apply)
51 52 53 54 55	Pupillary status	<input type="radio"/> Normal <input type="radio"/> Unilateral dilation <input type="radio"/> Bilateral dilation (If not detailed, choose "normal")
56 57 58 59 60	If abnormal pupillary status - reactive to light?	<input type="radio"/> Yes <input type="radio"/> No

16	Post-traumatic neurological deficit	<input type="checkbox"/> None of the below <input type="checkbox"/> Weakness in extremity <input type="checkbox"/> Numbness in extremity <input type="checkbox"/> Diplopia (double-vision) <input type="checkbox"/> Blurry vision <input type="checkbox"/> Dysphasia (problems with speech) <input type="checkbox"/> Dizziness / loss of balance <input type="checkbox"/> Loss of coordination <input type="checkbox"/> Other (Select all that apply. Do NOT check if patient had impairment prior to injury (e.g. already paralyzed patient))
14	If "other deficit" = yes, specify	_____
17	Other worrisome factors	<input type="checkbox"/> None of the below <input type="checkbox"/> Amnesia <input type="checkbox"/> Confirmed loss of consciousness <input type="checkbox"/> Suspected loss of consciousness (e.g. if patient is unsure) <input type="checkbox"/> Vomiting <input type="checkbox"/> Persistent headache <input type="checkbox"/> Seizure <input type="checkbox"/> Scalp wound that needed suturing (excl. face) <input type="checkbox"/> Suspected open or depressed skull fracture <input type="checkbox"/> Sign(s) of skull base fracture (Select all that apply)
30	If "amnesia" = yes, specify type(s)	<input type="radio"/> Retrograde (can't recall entire traumatic event) <input type="radio"/> Anterograde (can't remember new information) <input type="radio"/> Combined retrograde and anterograde <input type="radio"/> Unknown / missing
35	If "loss of consciousness" = yes, specify if it was due to the head injury (i.e. not syncope / fainting)	<input type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Unclear
40	If "vomiting" = yes, specify amount	<input type="radio"/> Once <input type="radio"/> More than once <input type="radio"/> Unknown / missing
44	If "sign(s) of skull base fracture" = yes, specify	<input type="checkbox"/> Racoon-eyes (bruising around eye - "black eye", "brillenhematoma") <input type="checkbox"/> Battle's sign (bruising of the mastoid process behind ear) <input type="checkbox"/> Rhinorrhea (CSF-leak from nose) <input type="checkbox"/> Otorrhea (CSF-leak from ear) <input type="checkbox"/> Anosmia (loss of smell) <input type="checkbox"/> Hematotympanon (blood behind ear drum) <input type="checkbox"/> Deafness <input type="checkbox"/> Nystagmus <input type="checkbox"/> Fascial nerve paralysis <input type="checkbox"/> Other
56	If "other sign(s) of skull base fracture" = yes, specify	_____
60	Lab sampled	<input type="radio"/> Yes <input type="radio"/> No

1 Date of lab sampling (first test)

2 \_\_\_\_\_  
3 (YYYY-MM-DD)  
4

5 Time of lab sampling (first test)

6 \_\_\_\_\_  
7 (HH:MM)  
8

9 S100B

10 \_\_\_\_\_  
11 (µg/L)  
12

13 PK(INR)

14 \_\_\_\_\_  
15

16 APT-time

17 \_\_\_\_\_  
18 (seconds)  
19

20 Hemoglobin (Hb)

21 \_\_\_\_\_  
22 (g/L)  
23

24 Platelet count

25 \_\_\_\_\_  
26 (150 x 10<sup>9</sup>/L)  
27

28 Serum ethanol

29 \_\_\_\_\_  
30 (mmol/L)  
31

32 Alcohol promille level (breathalyzer)

33 \_\_\_\_\_  
34 (promille)  
35

36 Date of CT scan

37 \_\_\_\_\_  
38 (YYYY-MM-DD)  
39

40 Time of CT scan

41 \_\_\_\_\_  
42 (HH:MM)  
43

44 Intracranial lesion on CT

45  Yes  No

46 If "intracranial lesion on CT" = yes, specify type(s)

- 47  Cerebral contusion  
48  Traumatic subarachnoid haemorrhage  
49  Epidural hematoma  
50  Acute subdural hematoma  
51  Chronic subdural hematoma  
52  Intraventricular hematoma  
53  Diffuse axonal injury  
54  Sinus thrombosis  
55  Traumatic infarct  
56  Skull fracture (neurocranium, not face)  
57 (Select all that apply)  
58  
59  
60

1 If "skull fracture" = yes, specify type(s)

- 2  Linear fracture with impression  
 3  Linear fracture without impression  
 4  Crush fracture with impression  
 5  Crush fracture without impression  
 6  Other

7 If "intracranial lesion on CT" = yes, specify  
 8 management

- 9  None (sent home from emergency department)  
 10  Admission < 48 hours due to TBI ("overnight  
 11 observation")  
 12  Admission > 48 hours due to TBI  
 13  Paus or reversal of anticoagulants or antiplatelets  
 14  Intubated due to TBI  
 15  Transfer to neurosurgical department  
 16  Death due to TBI  
 (Select all that apply)

17 If patient was admitted due to TBI, specify amount of  
 18 days in hospital

\_\_\_\_\_

19  
 20 Follow-up CT performed

Yes  No

21  
 22 If "follow-up CT performed" = yes, specify reason(s)

- 23  Decided on admission regardless of neurology  
 24  Decreased consciousness  
 25  Increased headache  
 26  New neurological abnormality  
 27  Vomiting  
 28  Other  
 29  Unclear / unknown

30  
 31 If "follow-up CT performed" = yes, specify if the  
 32 lesion progressed

Yes  No

33  
 34 Re-admission within 30 days with CT-verified  
 35 intracranial lesion

Yes  No





STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

## SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section	Item No	Description	Location
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	p. 1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	p. 3
	2b	All items from the World Health Organization Trial Registration Data Set	p. 3
Protocol version	3	Date and version identifier	N/A
Funding	4	Sources and types of financial, material, and other support	p. 11
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	p. 1
	5b	Name and contact information for the trial sponsor	N/A
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	N/A
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
<b>Introduction</b>			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	p. 4-5
	6b	Explanation for choice of comparators	N/A
Objectives	7	Specific objectives or hypotheses	p. 5
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	p. 5-8
<b>Methods: Participants, interventions, and outcomes</b>			

1		9	Description of study settings (eg, community clinic, academic hospital)	
2	Study setting		and list of countries where data will be collected. Reference to where list	p. 5-7
3			of study sites can be obtained	
4				
5	Eligibility	10	Inclusion and exclusion criteria for participants. If applicable, eligibility	
6	criteria		criteria for study centres and individuals who will perform the	p. 6
7			interventions (eg, surgeons, psychotherapists)	
8				
9		11a	Interventions for each group with sufficient detail to allow replication,	
10			including how and when they will be administered	N/A
11				
12		11b	Criteria for discontinuing or modifying allocated interventions for a given	
13			trial participant (eg, drug dose change in response to harms, participant	N/A
14			request, or improving/worsening disease)	
15	Interventions			
16		11c	Strategies to improve adherence to intervention protocols, and any	
17			procedures for monitoring adherence (eg, drug tablet return, laboratory	N/A
18			tests)	
19				
20		11d	Relevant concomitant care and interventions that are permitted or	
21			prohibited during the trial	N/A
22				
23				
24		12	Primary, secondary, and other outcomes, including the specific	
25			measurement variable (eg, systolic blood pressure), analysis metric (eg,	
26			change from baseline, final value, time to event), method of aggregation	
27	Outcomes		(eg, median, proportion), and time point for each outcome. Explanation	p. 7
28			of the clinical relevance of chosen efficacy and harm outcomes is	
29			strongly recommended	
30				
31				
32				
33	Participant	13	Time schedule of enrolment, interventions (including any run-ins and	
34	timeline		washouts), assessments, and visits for participants. A schematic	p. 10
35			diagram is highly recommended (see Figure)	
36				
37		14	Estimated number of participants needed to achieve study objectives	
38	Sample size		and how it was determined, including clinical and statistical assumptions	p. 8
39			supporting any sample size calculations	
40				
41				
42	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target	
43			sample size	p. 8
44				

#### Methods: Assignment of interventions (for controlled trials)

##### Allocation:

49		16a	Method of generating the allocation sequence (eg, computer-generated	
50			random numbers), and list of any factors for stratification. To reduce	
51	Sequence		predictability of a random sequence, details of any planned restriction	N/A
52	generation		(eg, blocking) should be provided in a separate document that is	
53			unavailable to those who enrol participants or assign interventions	
54				
55				
56	Allocation	16b	Mechanism of implementing the allocation sequence (eg, central	
57	concealme		telephone; sequentially numbered, opaque, sealed envelopes),	
58	nt		describing any steps to conceal the sequence until interventions are	N/A
59	mechanis		assigned	
60	m			

1	Implement	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A
2	ation			
3				
4	Blinding	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A
5	(masking)			
6				
7		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A
8				
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10				
11	<b>Methods: Data collection, management, and analysis</b>			
12				
13		18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	p. 8
14	Data			
15	collection			
16	methods			
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21		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A
22				
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26		19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	p. 6-7
27	Data			
28	management			
29				
30				
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32	Statistical	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	p. 8
33	methods			
34				
35				
36		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	N/A
37				
38				
39				
40		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	N/A
41				
42				
43				
44	<b>Methods: Monitoring</b>			
45				
46		21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N/A
47	Data			
48	monitoring			
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53		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	p. 8
54				
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56				
57		22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A
58	Harms			
59				
60				

1	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
2				
3				
4	<b>Ethics and dissemination</b>			
5				
6	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	p. 9
7				
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10				
11	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	N/A
12				
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14				
15				
16	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	N/A
17				
18				
19				
20		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
21				
22				
23	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	p. 7
24				
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27	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	p. 11
28				
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31	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	p. 7
32				
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35	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A
36				
37				
38				
39	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	p. 9
40				
41				
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44		31b	Authorship eligibility guidelines and any intended use of professional writers	N/A
45				
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48		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A
49				
50				
51	<b>Appendices</b>			
52				
53	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	N/A
54				
55				
56				
57	Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A
58				
59				
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1 \*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation &  
2 Elaboration for important clarification on the items. Amendments to the protocol should be tracked and  
3 dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-  
4 NonCommercial-NoDerivs 3.0 Unported](#)" license.  
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