

Biomarkers for RAtional Investigation for Neurological Decision Support in traumatic brain injury (BRaINS-TBI): cohort study with a nested pragmatic randomised controlled trial

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Last Edited 02/12/2025	Condition category Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Every year, over a million people in the UK go to the Emergency Department (ED) with a head injury. Most of these are mild, but some can lead to serious problems later. Right now, doctors use symptoms and CT scans to decide how serious the injury is, but this isn't always accurate. The BRaINS-TBI study is looking at whether a simple blood test can help doctors make better decisions. These tests look for "biomarkers" – tiny signals in the blood that may show if someone has a brain injury. The study also wants to find out if using these tests can improve care and reduce unnecessary scans.

Who can participate?

People who come to the ED with a mild head injury may be invited to take part. The study also includes healthy volunteers and people with other types of injuries (not involving the head) to help compare results.

What does the study involve?

Participants may be asked to give a blood sample and share information about their injury and recovery. Some people will be randomly chosen to have their blood test results shared with their doctor to help guide care.

Follow-up will happen over the next six months, either by phone, online questionnaires, or in-person visits.

What are the possible benefits and risks of participating?

Taking part could help improve how head injuries are treated in the future. It may also help reduce unnecessary CT scans and improve long-term outcomes.

Risks are low – giving a blood sample is safe, and all personal information will be kept confidential. Participation is voluntary, and people can leave the study at any time.

Where is the study run from?
University of Cambridge (UK)
Cambridge University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
October 2025 to December 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
Dr Emma Flanagan, e.flanagan@uea.ac.uk

Contact information

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Public, Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
354593

National Institute for Health and Care Research (NIHR)
159241

Central Portfolio Management System (CPMS)
57709

Study information

Scientific Title

Biomarkers for RAtional Investigation for Neurological Decision Support in traumatic brain injury (BRaINS-TBI): cohort study with a nested pragmatic randomised trial

Acronym

BRaINS-TBI

Study objectives

We aim to carry out a large study across multiple hospitals to find out whether certain substances in the blood (called biomarkers) can help predict how people will recover in the months after a mild traumatic brain injury (mTBI). The study also includes a smaller randomised trial to test whether two specific blood biomarkers (UCH-L1 and GFAP), when used together with existing clinical guidelines (the NICE head injury rules), can help doctors decide more accurately who needs a CT brain scan.

1. In adults who present to an ED with a head injury, can biomarkers be used to identify patients at high risk of ongoing problems and so help to rationally assign patients to ongoing clinical care and follow up pathways?
2. Can biomarkers be used to identify which patients require a CT head to rule out a clinically important intracranial injury?

Ethics approval required

Ethics approval required

Ethics approval(s)

submitted 01/10/2025, East of England - Essex Research Ethics Committee (2 Redman Place, London, EC20 1 JQ, United Kingdom; +44 207 104 8106; essex.rec@hra.nhs.uk), ref: 25/EE/0233

Study design

Multi-centre prospective observational cohort study with nested interventional randomized controlled trial

Primary study design

Interventional

Study type(s)

Diagnostic, Screening

Health condition(s) or problem(s) studied

Traumatic brain injury

Interventions

BRaINS-TBI has two components:

1. BRaINS-TBI Predict – a prospective observational cohort study.
2. BRaINS-TBI CT – a nested pragmatic randomised controlled trial evaluating the impact of using i-STAT TBI test biomarker results to support CT decision-making in the emergency department (ED).

For the nested randomised controlled trial (BRaINS-TBI CT):

Aim: To determine whether integrating i-STAT biomarker results with existing NICE CT head rules improves decision-making regarding CT scanning in adults with mild TBI.

Study arms:

Arm A: Biomarker-Informed Pathway (Intervention Arm)

Participants receive standard NHS care plus the i-STAT TBI test.

The biomarker results (UCH-L1 and GFAP) are released to the treating ED clinician in real time and may be used alongside NICE guidance to support the decision on whether to perform a CT head scan.

All other aspects of care follow standard clinical practice.

Arm B: Standard Care Pathway (Control Arm)

Participants receive standard clinical assessment and management according to NICE NG232 Head Injury Guidelines.

The biomarker sample is still taken for research purposes, but results are not made available to the clinical team at the point of care and do not influence treatment, with participants in this arm having decisions for CT made according to standard care.

Randomisation Process

Eligible participants are randomised in the ED using a secure web-based randomisation system managed by the Norwich Clinical Trials Unit.

Randomisation is 1:1, stratified by site, and uses variable block sizes to ensure allocation concealment.

The trial is unblinded due to the nature of the intervention (clinicians must know whether biomarker results are available).

Follow-up Duration for both RCT arms

Participants in both arms are followed for 6 months, at the same time points and using the same outcome measures as the observational cohort:

2–4-week follow-up

3-month follow-up

6-month follow-up

Follow-up includes validated and exploratory questionnaires, resource-use data, and clinical outcome measures such as the GOSE.

Intervention Type

Device

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Abbott i-STAT™ Alinity System (i-STAT TBI test cartridge)

Primary outcome(s)

For the observational cohort (BRaINS-TBI Predict):

Extended Glasgow Outcome Scale (GOSE) at six months. For analysis GOSE will be dichotomised as GOSE<8 (GOSE 1-7 vs 8) which is often described as incomplete recovery versus complete recovery.

For the randomised trial (BRaINS-TBI CT):

Percentage of patients with computed tomography (CT) scans of the head (brain) ordered to rule out a clinically significant intracranial lesion during the Emergency Department visit.

Key secondary outcome(s)

For the observational cohort (BRaINS-TBI Predict):

Glasgow Outcome Score Extended (GOSE) at 6 months dichotomised into other commonly used categories (GOSE≤6

(GOSE 2-6 vs 7-8), and GOSE≤4 (GOSE 2-4 vs 5-8). Three-month GOSE, symptom type + burden from RPQ and PRS, quality of life, mental health and neurocognitive function. These other outcome measures will be used to assess for ceiling effects in GOSE as well as ensuring outcomes important to patients are assessed.

Planned subgroup analyses: Sex, >65 years, major extracranial injury, renal dysfunction (eGFR) and significant co-morbidities (e.g. dementia, other neurological disease). Effect of timing of blood sampling (<6 hours, <12 hours, 12 to 24 hours) and effect of two blood samples.

For the randomised trial (BRaINS-TBI CT):

Deterioration up to 30 days after ED attendance. A planned composite outcome measure will be comprised of: death attributable to TBI within 30 days of first presentation, requirement for neurosurgical intervention, seizure, neurological deterioration (new deficit or drop in GCS of more than 2 points), intensive care unit (ICU) admission for TBI, intubation recorded within 30 days of first presentation, or hospital readmission for TBI within 30 days of first presentation. Where reason for death, ICU admission, or readmission is unknown, it will be attributed to TBI deterioration. To ensure that no signal of harm is missed each component will be assessed individually as well as the overall composite measure.

Completion date

31/12/2027

Eligibility

Key inclusion criteria

BRaINS-TBI Predict (Observational Cohort Study)

Patients who have sustained a head injury:

1. ≥ 16 years of age
2. Glasgow Coma Score 13, 14, or 15
3. Presentation within 24 hours of sustaining a head injury
4. Meet criteria to be assessed for consideration of a head CT using NICE NG232 clinical decision support tool (CDST).
5. Patients with a prior history of TBI which required clinical assessment but occurred more than 1 year prior may still be included.

Non-head injury trauma patient controls:

6. ≥ 16 years of age
7. Glasgow Coma Score 15 or at cognitive baseline
8. Presentation within 24 hours of trauma to part of body other than head. No head injury noted by patient and/or witnesses

Healthy Volunteers:

9. Adult ≥ 16 years of age

BRaINS-TBI CT (Nested RCT):

1. ≥ 18 years of age
2. Glasgow Coma Score 13, 14, or 15
3. Presentation within 24 hours of head injury
4. When assessed using NICE NG232 clinical decision support tool (CDST) found to have loss of consciousness or amnesia plus any of
 - 4.1. Age 65 years or over
 - 4.2. Any bleeding or clotting disorders (liver failure, haemophilia, taking anticoagulants or antiplatelets)
 - 4.3. Dangerous mechanism of injury (a pedestrian or cyclist struck by a motor vehicle, an occupant ejected from a motor vehicle, or fall from a height of more than 1m or 5 stairs)
 - 4.4. More than 30 minutes' retrograde amnesia of events immediately before the head injury
 - 4.5. Subjects on anticoagulant or antiplatelet agents, excluding aspirin monotherapy, with no other high or medium risk features and shared decision making positive for CT

Participant type(s)

Healthy volunteer, Patient

Healthy volunteers allowed

No

Age group

Mixed

Lower age limit

16 years

Upper age limit

100 years

Sex

All

Total final enrolment

0

Key exclusion criteria

BRaINS-TBI Predict (Observational Cohort Study)

Patients who have sustained a head injury:

1. Participant without capacity and no available patient legal representative or professional consultee available.
2. Participant with capacity unwilling to provide informed consent
3. Unable to adequately understand written and verbal English for consent and assessments unless an appropriate translator is available.

Non-head injury trauma patient controls:

4. Any evidence of a current head injury
5. History of a previous head injury requiring medical care.
6. Participant without capacity and no available patient legal representative or professional consultee.
7. Participant with capacity unwilling to provide informed consent
8. Unable to adequately understand written and verbal English for consent and assessments unless an appropriate translator is available.

Healthy Volunteers:

9. Prior history of head injury/traumatic brain injury requiring medical assessment or care
10. Other significant neurological disease requiring ongoing treatment/management

BRaINS-TBI CT (Nested RCT):

1. Low risk TBI according to NICE-CDR
2. Significant extra-cranial injury for which a full trauma CT would usually be indicated.
3. Any NICE Guideline (NG232) high risk criteria
 - 3.1. GCS \leq 12 on initial assessment in the ED (aside from intoxicated subjects with no other concerning features)
 - 3.2. Suspected open or depressed skull fracture
 - 3.3. Any sign of basal skull fracture (haemotympanum, 'panda' eyes, cerebrospinal fluid leakage from the ear or nose, Battle's sign)
 - 3.4. Post-traumatic seizure
 - 3.5. Focal neurological deficit
 - 3.6. More than 1 episode of vomiting

Date of first enrolment

01/12/2025

Date of final enrolment

30/06/2027

Locations

Countries of recruitment

United Kingdom

England

Scotland

Wales

Study participating centre

Cambridge University Hospitals NHS Foundation Trust

Cambridge Biomedical Campus

Hills Road

Cambridge

England

CB2 0QQ

Study participating centre

NHS Grampian

Summerfield House

2 Eday Road

Aberdeen

Scotland

AB15 6RE

Study participating centre

University Hospitals of Derby and Burton NHS Foundation Trust

Royal Derby Hospital

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DE22 3NE

Study participating centre

Greater Glasgow and Clyde

Gartnavel Royal Hospital

1055 Great Western Road

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G12 0XH

Study participating centre

Liverpool University Hospitals NHS Foundation Trust
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Prescot Street
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L7 8XP

Study participating centre

Oxford University Hospitals NHS Foundation Trust
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Study participating centre

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M6 8HD

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S5 7AU

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Barts Health NHS Trust
The Royal London Hospital
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Study participating centre
Swansea Bay University Local Health Board
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Sponsor information

Organisation

University of Cambridge

ROR

<https://ror.org/013meh722>

Organisation

Cambridge University Hospitals NHS Foundation Trust

Funder(s)**Funder type**

Government

Funder Name

Efficacy and Mechanism Evaluation Programme

Alternative Name(s)

NIHR Efficacy and Mechanism Evaluation Programme, Efficacy and Mechanism Evaluation (EME), EME

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications**Individual participant data (IPD) sharing plan**

De-identified participant data (demographics, biomarker results, CT findings, outcomes) will be shared after publication of primary analyses via the secure UK TBI-REPORTER data repository (<https://tbi-reporter.uk/>). Access will be granted to researchers for ethically approved studies in line with NIHR and sponsor data-sharing policies. Supporting documents (protocol, SAP, data dictionary) will be available on request from NCTU.

IPD sharing plan summary

Stored in publicly available repository