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

Submission date
03/11/2025

Recruitment status
Not yet recruiting

Registration date
18/11/2025

Overall study status
Ongoing

Last Edited
22/01/2026

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] 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 ≤ 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
19/02/2026

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
Uttoxeter Road
Derby
England
DE22 3NE

Study participating centre
Greater Glasgow and Clyde
Gartnavel Royal Hospital
1055 Great Western Road

Glasgow
Scotland
G12 0XH

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
England
L7 8XP

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
England
OX3 9DU

Study participating centre
University Hospitals Plymouth NHS Trust
Derriford Hospital
Derriford Road
Derriford
Plymouth
England
PL6 8DH

Study participating centre
Royal Berkshire NHS Foundation Trust
Royal Berkshire Hospital
London Road
Reading
England
RG1 5AN

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal

Stott Lane
Salford
England
M6 8HD

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
England
S5 7AU

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
80 Newark Street
London
England
E1 2ES

Study participating centre
Swansea Bay University Local Health Board
Tonna Hospital
Tonna Uchaf
Tonna
Neath
Wales
SA11 3LX

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
England
NR4 7UY

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