

# Mild traumatic brain injury biomarker study, a prospective cohort biomarker study of military and civilian participants with mild traumatic brain injury

<b>Submission date</b> 13/04/2023	<b>Recruitment status</b> Recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 21/08/2023	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Protocol
<b>Last Edited</b> 07/10/2025	<b>Condition category</b> Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

There are over a million hospital visits each year in the UK for mild traumatic brain injury (mTBI), sometimes called concussion. Although it is classed as mild, a third of patients can't work a year after their injury; it leads to a disproportionate impact on future health. Mild traumatic brain injury can be caused by physical impact to the head through accident, injury or sport, or due to the effects on the brain of shockwaves caused by explosions.

The consequences of mTBI are profound, with many patients suffering long-term disability due to persistent headaches, imbalance, memory disturbance and poor mental health. We can't yet identify those most at risk of these disabling consequences. This is a clear unmet need which would allow the targeting of treatments to improve patient outcomes. The main aim of this study is to develop a predictive biomarker model for outcomes after mTBI.

### Who can participate?

Patients aged between 18 and 60 years (inclusive) with confirmed mild traumatic brain injury within the last 3 months can participate in the main study.

Any member of the public aged between 18 and 60 years (inclusive) without confirmed mild traumatic brain injury can participate in the case-control and biological variability substudies.

### What does the study involve?

The mTBI participants will have in-person assessments (clinical and imaging) at baseline (both 21 days and 3 months after mTBI), with remote follow-up continuing until 2 years after mTBI. 40 mTBI participants will repeat either the baseline clinical assessments or baseline imaging assessments 4 times within 12 days, as part of the biological variability sub-study.

Patients can be recruited at three points after injury: 0-24 hours post-injury, 21 days post-injury, or 3 months post-injury. The total number of visits will vary depending on the point of study entry.

The first 40 healthy volunteers will repeat either all clinical assessments four times within 12 days, or all imaging assessments six times within 19 days, as part of the biological variability sub-

study. The remaining healthy volunteers will have a baseline (clinical and imaging assessment) and limited remote follow-up for 3 months.

All baseline (21-day and 3-month) assessments, whether clinical or imaging, will be the same for mTBI participants and healthy volunteers.

What are the possible benefits and risks of participating?

For mTBI patients, there is the potential that they will receive a more in-depth post-injury follow-up than would normally be the case. Otherwise, there is not expected to be any direct benefit.

As there is no intervention involved in this study the risks are considered minimal. There is a risk of adverse effects related to the study procedures:

1. Bruising from taking blood samples
2. Discomfort/feeling of claustrophobia from MRI scanners
3. Feelings of nausea from vestibular assessment

Where is the study run from?

University of Birmingham Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?

September 2021 to November 2029

Who is funding the study?

Ministry of Defence (UK)

Who is the main contact?

Ryan Ottridge and Andy Palmer, mTBI-Predict@bham.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Mr Andrew Palmer

### Contact details

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mtbi-predict@trials.bham.ac.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Integrated Research Application System (IRAS)

319062

**Protocol serial number**

RG\_22-004, IRAS 319062, CPMS 56875

## Study information

**Scientific Title**

Mild traumatic brain injury biomarker study, a prospective cohort biomarker study of military and civilian participants with mild traumatic brain injury (mTBI-Predict)

**Acronym**

mTBI-Predict

**Study objectives**

Mild traumatic brain injury (mTBI) (sometimes called concussion) is common with over 1 million hospital visits due to mTBI each year in the UK. Although classed as mild, it leads to a disproportionate impact on future health, with 3 in 10 patients unable to work 12 months after their injury.

This study will test key biomarkers to allow the identification of mTBI patients at risk of long-term health issues. Biomarkers need to be accurate, reproducible and practical to use in a clinical setting.

The researchers will conduct a long-term study following patients after a new mTBI. At the onset, they will measure a variety of different, but complementary biomarkers including brain imaging, brain physiology, blood and saliva, headache, mental health, vision, balance and cognitive performance. The researchers will then look at the ability of these biomarkers to predict long-term complications at 6, 12 and 24 months post-injury. This will allow those with a good prognosis to rapidly return to service/work/play and those likely to suffer complications to receive prompt and targeted therapy.

**Ethics approval required**

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**Ethics approval(s)**

approved 09/05/2023, Ministry of Defence Research Ethics Committee (Defence Science and Technology, Dstl Portsdown West, Fareham, PO17 6AD, United Kingdom; +44 (0)300 153 5372; DST-MODRECTeam@mod.gov.uk), ref: 2217/MODREC/23

**Study design**

Longitudinal prospective cohort study with nested variability and case-control studies in military and civilian populations including impact, blast and sports injury

**Primary study design**

Observational

**Study type(s)**

Other

## **Health condition(s) or problem(s) studied**

Mild traumatic brain injury

## **Interventions**

The 610 mTBI participants will have in-person assessments (clinical and imaging) at baseline (both 21 days and 3 months after mTBI), with remote follow-up continuing until 2 years after mTBI. 40 mTBI participants will repeat either the baseline clinical assessments or baseline imaging assessments 4 times within 12 days, as part of the biological variability sub-study.

Patients can be recruited at three points after injury: 0-24 hours post-injury, 21 days post-injury, or 3 months post-injury. The total number of visits will vary depending on the point of trial entry.

The first 40 healthy controls will repeat either all clinical assessments four times within 12 days, or all imaging assessments six times within 19 days, as part of the biological variability sub-study. The remaining healthy controls will have a baseline (clinical and imaging assessment) and limited remote follow-up for 3 months.

All baseline (21-day and 3-month) assessments, whether clinical or imaging, will be the same for mTBI participants and healthy control volunteers.

## **Intervention Type**

Other

## **Primary outcome(s)**

The ability of candidate biomarkers to predict full return to play, work or duty at 6 months post-injury, measured using:

1. Headache: patient-completed headache diary
2. Mental Health: Post-Traumatic Stress Disorder checklist
3. Vestibular: vestibular perceptual thresholds
4. Cognition: Corrected Global Composite Score
5. Visual: retinal nerve fibre layer thickness
6. Imaging: MRI, magnetoencephalography (MEG)
7. Hormone/biofluids: cortisol, glial fibrillary acidic protein
8. Cerebral physiology: cerebrovascular reactivity, physical function tests

## **Key secondary outcome(s)**

The ability of candidate biomarkers to predict global function, persistent post-traumatic headache, cognitive dysfunction, depression, PTSD, vestibular disturbances and physical function at 6 months, measured using:

1. Headache: patient-completed headache diary
2. Mental Health: Post-Traumatic Stress Disorder checklist
3. Vestibular: vestibular perceptual thresholds
4. Cognition: Corrected Global Composite Score
5. Visual: retinal nerve fibre layer thickness
6. Imaging: MRI, magnetoencephalography (MEG)
7. Hormone/biofluids: cortisol, glial fibrillary acidic protein
8. Cerebral physiology: cerebrovascular reactivity, physical function tests

Exploratory outcomes:

Accuracy of a multifaceted computer-modelled biomarker algorithm to predict sequelae of mTBI (full return to play, work or duty, persistent post-traumatic headache, cognitive dysfunction,

depression, PTSD, vestibular disturbances, and physical function) using computer modelling at 6 months post-injury

**Completion date**

30/11/2029

## Eligibility

**Key inclusion criteria**

Main study:

1. Aged  $\geq 18$  and  $\leq 60$  years
2. mTBI: acute (<3 months) mild traumatic brain injury (as per VA/DoD criteria)

Healthy controls:

1. Aged  $\geq 18$  years and  $\leq 60$  years
2. Healthy (screened through NHS General Health Questionnaire)

**Participant type(s)**

Mixed

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Upper age limit**

60 years

**Sex**

All

**Key exclusion criteria**

Main study:

1. Prior diagnosis of PTSD or severe mental illness (e.g. bipolar disorder or psychosis)
2. Pregnancy
3. Prior brain injury (from trauma, stroke or other aetiologies) without full functional and symptomatic recovery
4. Inability to comply with study schedule or follow-up
5. Inability to provide informed consent (e.g. due to cognitive impairment)
6. Any progressive neurodegenerative or neuroinflammatory condition
7. Alcohol use disorder or drug dependence
8. Patients with medical conditions that are unstable or untreated

Healthy controls:

1. Medical condition requiring treatment or significant past medical history
2. Prior diagnosis of PTSD or severe mental illness

3. Pregnancy
4. Prior brain injury (from trauma, stroke or other aetiologies) without full functional and symptomatic recovery
5. Inability to comply with study schedule or follow-up
6. Inability to provide informed consent (e.g. due to cognitive impairment)
7. Inability to safely enter the MRI environment (for imaging variability and case-control study)
8. Any progressive neurodegenerative or neuroinflammatory condition
9. Cardiovascular or cerebrovascular disease or hypertension (no current diagnosis/medication)
10. Alcohol use disorder or drug dependence
11. Patients with medical conditions that are unstable or untreated
12. History of pituitary hormone deficits

**Date of first enrolment**

01/06/2023

**Date of final enrolment**

31/05/2027

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**University Hospitals Birmingham NHS Foundation Trust**

Queen Elizabeth Hospital

Mindelsohn Way

Edgbaston

Birmingham

United Kingdom

B15 2GW

**Study participating centre**

**University of Nottingham**

University Park

Nottingham

United Kingdom

NG7 2RD

**Study participating centre**

**Aston University**

The Aston Triangle

Birmingham

United Kingdom  
B4 7ET

## Sponsor information

### Organisation

University of Birmingham

### ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Government

### Funder Name

Ministry of Defence

### Alternative Name(s)

MOD

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date.

### IPD sharing plan summary

Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
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[Study website](#)

Study website

11/11/2025

11/11/2025

No

Yes