Investigating imaging and clinical decision tools for identifying and ruling out subarachnoid haemorrhage in patients presenting with an acute severe headache to UK Emergency Departments

Submission date 14/10/2020	Recruitment status No longer recruiting	[X] Prospectively registered		
		[X] Protocol		
Registration date	Overall study status	Statistical analysis plan		
17/11/2020	Completed	[_] Results		
Last Edited 09/08/2022	Condition category Circulatory System	Individual participant data		
		[] Record updated in last year		

Plain English summary of protocol

Background and study aims

The SHED study aims to understand how acute headaches are dealt with by the Emergency Department (ED). It wants to understand how accurate the investigations for identifying and ruling out a bleed on the brain, called a subarachnoid haemorrhage are.

Who can participate?

Any adult with an acute severe headache that reached maximal intensity within one hour presenting to UK Emergency Departments (ED) between October 2021 and February 2022

What does the study involve?

This study doesn't involve any additional treatments or tests, and no extra questions other than those that the participant's doctor will ask you routinely. The study team are not seeking written consent for this study because it involves no change in patient clinical assessment or care. However, if participants do not want to take part it is easy to opt-out as described at http://ternresearch.co.uk.

What are the possible benefits and risks of participating? There will be no direct benefit to participants from taking part. However, this research may change the way that headaches are managed in the future and therefore impact future treatment for those who re-attend. It could also positively impact other patients who come to the hospital with the same problem.

As part of routine care participant's doctor may decide you need a CT Brain and/or CT angiography as part of your routine care. Those who take part in this study will not undergo any additional x-ray imaging. These procedures use ionising radiation to form images of your body and provide the doctor with other clinical information. Ionising radiation can cause cell damage

that may, after many years or decades, turn cancerous. The chances of this happening to participants are the same whether they take part in this study or not. There is also a risk within the study of data storage. The study team have minimised this risk through use of a specialist medical database service which conforms to all current international standards. This project will be treated like any serious research study, with strict oversight and regular review.

Where is the study run from? The Northern Care Alliance (UK) with data collected from over 100 UK emergency departments.

When is the study starting and how long is it expected to run for? August 2019 to February 2023

Who is funding the study? The Royal College of Emergency Medicine (UK)

Who is the main contact? Dr Robert Hirst tern@rcem.ac.uk

Study website http://ternresearch.co.uk/SHED

Contact information

Type(s) Scientific

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Additional identifiers

EudraCT/CTIS number Nil known

IRAS number

ClinicalTrials.gov number Nil known

Secondary identifying numbers Nil known

Study information

Scientific Title Subarachnoid Haemorrhage in the Emergency Department (SHED)

Acronym SHED

Study objectives

To understand the sensitivity of CT brain and the Ottawa subarachnoid clinical decision rule for patients presenting with acute severe headache (with maximal intensity within 1 h) to UK Emergency Departments.

Ethics approval required Old ethics approval format

Ethics approval(s)

Approved 11/02/2020, South West Frenchay Research Ethics Committee (Level 3, Block B Whitefriars Lewins Mead, Bristol BS1 2NT; nrescommittee.southwest-frenchay@nhs.net; +44 (0) 207 104 8290), ref: 19/SW/0243

Study design Prospective observational cohort study

Primary study design Observational

Secondary study design

Cohort study

Study setting(s)

Hospital

Study type(s) Diagnostic

Participant information sheet

Available from http://ternresearch.co.uk, See additional file ISRCTN18417679_PIS_v1. 1_5Dec2019 (added 02/12/2020)

Health condition(s) or problem(s) studied

Subarachnoid haemorrhage and acute severe headache

Interventions

As an observational study, there will be no change to clinical practice. Headache features will be prospectively collected. Relevant investigations of CT brain, lumbar puncture, and CT-angiogram will be collected. 28-day follow-up data for subarachnoid haemorrhage and mortality will be collected.

Subarachnoid haemorrhage will be identified from the data collected as any of the following: 1. Subarachnoid Blood present on unenhanced CT reported by a trained radiologist. Site CT characteristics will be collected to include minimum criteria applied for inclusion in the final analysis, as follows:

- 1.1. A 3rd generation multi-slice scanner (4 to 320 slices/rotation)
- 1.2. 5-7.5 mm cuts for brain
- 1.3. 2.5 5mm cuts for the posterior fossa

2. Subarachnoid Blood present on CT-Angiogram or MR-Angiogram reported by a trained radiologist

3. CSF findings consistent with SAH according to the 2008 National Biochemist reporting guideline. The vast majority of UK laboratories processing CSF samples adhere to the 2008 clinical biochemistry guidelines. However, for those sites identified as using xanthochromia or red blood cells in lieu of 2008 criteria, the study team will adopt criteria stipulated in the original paper by Perry et al.

4. Visible xanthochromia. Red blood cells (>5×106/L) in the final tube of cerebrospinal fluid collected and an aneurysm identified on cerebral angiography (digital subtraction, computed tomography, or magnetic resonance angiography)

All cases of subarachnoid haemorrhage within the cohort will be captured, by performing follow up at 28 days from presentation. Clinical notes and primary care contact will be scrutinised, to determine reference standard diagnosis, clinical outcomes and mortality. HES data will be pursued using the 4 digit diagnostic codes for subarachnoid haemorrhage following database lock.

Intervention Type

Other

Primary outcome measure

Current primary outcome measure as of 18/05/2021:

1. External validation of a 6-hour CT brain rule out strategy for alert (defined as awake and fully orientated or GCS 15/15) patients presenting with acute non-traumatic headache, where there is clinical concern for SAH using prospectively collected data.

Previous primary outcome measure:

1. External validation of the proposed 6 h CT brain rule out strategy for alert patients (defined as awake and fully orientated or GCS 15/15) presenting with acute non-traumatic headache, suggestive of subarachnoid haemorrhage using prospectively collected data

Secondary outcome measures

1. Change in sensitivity of CT brain imaging in patients presenting with acute severe headache over hourly intervals from 6 to 24 h after onset of headache using prospectively collected CT brain data

2. Validation of the Ottawa subarachnoid haemorrhage clinical decision rule in patients presenting with acute non-traumatic headache using prospectively collected clinical notes, primary care contact data, and HES data

Added 18/05/2021:

The prevalence of subarachnoid haemorrhage in patients under 40 years of age identified from the data collected as any of the following:

1. Subarachnoid blood present on unenhanced CT reported by a trained radiologist. Site CT characteristics will be collected to include minimum criteria applied for inclusion in the final analysis, as follows:

1.1. A 3rd generation multi-slice scanner (4 to 320 slices/rotation)

1.2. 5 – 7.5 mm cuts for brain

1.3. 2.5 – 5 mm cuts for the posterior fossa

2. Subarachnoid blood present on CT-angiogram or MR-angiogram reported by a trained radiologist

3. CSF findings consistent with SAH according to the 2008 National Biochemist reporting guideline. The vast majority of UK laboratories processing CSF samples adhere to the 2008 clinical biochemistry guidelines. However, for those sites identified as using xanthochromia or red blood cells in lieu of 2008 criteria, the study team will adopt criteria stipulated in the original paper by Perry et al.

4. Visible xanthochromia. Red blood cells (>5 × 10e6/l) in the final tube of cerebrospinal fluid collected and an aneurysm identified on cerebral angiography (digital subtraction, computed tomography, or magnetic resonance angiography)

For patients who are evaluated for acute severe headache reaching maximal intensity within 1 hour in UK emergency departments.

Overall study start date

01/08/2019

Completion date 01/02/2023

Eligibility

Key inclusion criteria

1. Aged ≥18 years

2. Presenting with a non-traumatic acute headache that reaches maximal intensity within one hour to UK Emergency Departments (ED) or equivalent acute secondary care environment

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

9,000

Key exclusion criteria

- 1. Direct head trauma in the previous 7 days
- 2. Returning for reassessment of the same headache within the recruitment period
- 3. Established diagnosis of subarachnoid haemorrhage, brain neoplasm, ventricular shunt or

hydrocephalus prior to attendance at the emergency department.

4. Focal neurological deficit

5. Headache with onset >14 days prior to attendance

6. Recurrent headaches defined as ≥3 headaches of similar character and intensity as presenting headache

- 7. Transfer from another hospital with confirmed subarachnoid haemorrhage
- 8. Prisoner presenting to ED/secondary care
- 9. Patient currently under detained Mental health act, presenting to ED/secondary care

Date of first enrolment

01/10/2021

Date of final enrolment 01/02/2023

Locations

Countries of recruitment England

United Kingdom

Study participating centre North Bristol NHS Trust Bristol Bristol United Kingdom BS10 5NB

Sponsor information

Organisation Northern Care Alliance

Sponsor details Salford Royal NHS Foundation Trust Summerfield House 544 Eccles New Road Salford England United Kingdom M5 5AP +44 (0)161 206 5235 Steve.Woby@srft.nhs.uk

Sponsor type Hospital/treatment centre

Funder(s)

Funder type University/education

Funder Name Royal College of Emergency Medicine

Alternative Name(s) RCEM

Funding Body Type Private sector organisation

Funding Body Subtype Universities (academic only)

Location United Kingdom

Results and Publications

Publication and dissemination plan

The results from this study will be submitted for publication in leading journals and to national conferences for presentation. The Trainee Emergency Research Network (TERN) aims to be a promoting force for research opportunity in emergency medicine and will be providing regular input to the national academic conference agenda for emergency medicine, to highlight recent projects, ongoing work and opportunity for submission of ideas. 29

In addition, this project offers the opportunity for TERN to develop a national strategy with regards to project output and knowledge translation. Recent collaborations with online learning resources ensure that this project will be regularly appraised and updated throughout delivery, through a dedicated TERN section on this college website.

TERN will also aim to develop a local dissemination strategy using trainees to highlight findings and implement change where relevant within local departments. Free Open Access Medical Education channels will be used to highlight and appraise the project results. Blogs, podcasts and discussions will be planned to highlight lessons learned about trainee networks research and cloud-based data collection.

Intention to publish date

30/05/2023

Individual participant data (IPD) sharing plan

Data will be stored using a non-publically available repository, REDCap. Data will be collected by local clinicians who would usually have access to the data as part of routine clinical care and stored within local medical records. Data entered into the online database will be encrypted, password protected and only identifiable to the local care team and the Chief Investigators for the purposes of data validation only. Local data collectors will only have access to their own site data when they access the database.

Patient-level data will only be reviewed by the local direct healthcare/research nursing team and stored in a manner compliant with standard medical record procedure at the local hospitals. Anonymised clinical data will be extracted and uploaded to a secure and GCP compliant online database (REDCAP). Any personal identifiers used to generate an anonymised medical record on the database will be encrypted and only be accessed by the study Chief Investigator or members of the direct healthcare team, for review only in the event of data queries.

The fully anonymised dataset will be locked and analysed by Dr William Hulme, statistician at the University of Manchester. Study data will stored on the REDCAP database for 5 years. Individual sites will retain screening logs with identifiable data on-site for a period of 5 years after the study has closed to recruitment, to ensure any data queries or source data validation exercises can be completed. This information will be stored locally by clinical care and/or research teams, in compliance with local organizational procedures.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.1	05/12/2019	02/12/2020	No	Yes

Protocol preprint

<u>Protocol (preprint)</u>	06/10/2021	No	No
HRA research summary	28/06/2023	No	No