# Cluster randomised trial of an intervention to promote implementation of clinical guidance on the management of suspected encephalitis

Submission date	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered		
22/07/2013		[X] Protocol		
Registration date 22/07/2013	Overall study status Completed	Statistical analysis plan		
		[X] Results		
Last Edited	Condition category	Individual participant data		
11/12/2018	Infections and Infestations			

#### Plain English summary of protocol

Background and study aims

Up to twenty eight hospitals will be recruited across the UK to take part in this study which will evaluate the effects of an intervention to improve the clinical management of patients with suspected encephalitis (inflammation of the brain) in secondary care. This will involve assessing adherence to the national guidelines for encephalitis and developing and applying an intervention to improve adherence. The development of the intervention will be informed by existing evidence on professional behaviour change and sub-studies within the ENCEPH UK programme. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. Cost effectiveness and clinical outcomes will be assessed. The study aims to give clinicians evidence-based tools to help them implement the national guidance for management of suspected encephalitis patients.

## Who can participate?

Any patients in whom encephalitis should have been suspected within the recruited sites will be included in the study.

#### What does the study involve?

Hospitals will be randomly allocated to either the standard care group or the intervention group. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. Nurses will collect data from the patients' notes and this will be recorded on the data collection forms in a similar style to a clinical audit. No identifiable data such as name or NHS number will be recorded; the patients' date of birth and gender will be collected so that we can categorise the population. The hospital will keep the key of which patient has been allocated to each number so that data queries can be checked; however, this encryption key will remain at the hospital.

What are the possible benefits and risks of participating? Ideally, all hospitals should be following accepted best practice in the care of suspected

encephalitis. However, we know this is not the case. Should the intervention be effective, patient care in intervention hospitals should improve. We do not foresee any additional risks to patients in either group of the study.

Where is the study run from?

This study is being run by Brain Infections UK within The University of Liverpool. Up to 28 hospitals will be recruited across the UK.

When is the study starting and how long is it expected to run for? This study is due to start data collection in January 2014 and will run for a further 2 years.

Who is funding the study? National Institute of Health Research (UK).

Who is the main contact?
Prof Tom Solomon, Chief Investigator
Dr Ruth Backman, Trial Coordinator, R.Backman@liverpool.ac.uk

## Contact information

#### Type(s)

Scientific

#### Contact name

Dr Ruth Backman

#### Contact details

Trial Coordinator ENCEPH UK Intervention RCT Institute of Infection and Global Health Ronald Ross Building University of Liverpool 8 West Derby Street Liverpool United Kingdom L69 7BE

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## Additional identifiers

**EudraCT/CTIS** number

**IRAS** number

ClinicalTrials.gov number

Secondary identifying numbers 14688

## Study information

#### Scientific Title

Development and evaluation of an intervention based around the national guidelines on the management of suspected encephalitis, and its evaluation through a cost-effectiveness analysis

#### Acronym

**ENCEPH UK Intervention RCT** 

#### **Study objectives**

Up to 28 hospitals will be recruited across the UK to take part in this cluster randomised controlled trial which will evaluate the effects of an intervention to improve the clinical management of suspected encephalitis in secondary care. The cost effectiveness of the intervention will also be assessed. The study will be run over two years including a 12-month follow-up intervention period.

Within this study we will compare the rate of diagnosis for encephalitis between the 'routine' hospitals and intervention hospitals. The development of the intervention will be informed by existing evidence on professional behaviour change and sub-studies within the ENCEPH UK programme. The intervention will target clinicians responsible for the diagnosis and initial management of suspected encephalitis. The use of a cluster randomised controlled trial in up to twenty eight hospitals with a follow-up period of 12 months will allow both cost effectiveness and clinical outcomes to be assessed.

The main outcome will be the proportion of patients with suspected encephalitis appropriately investigated and started on treatment with aciclovir within 6 hours and those patients that had a lumbar puncture performed within 12 hours (unless it was clinically contraindicated).

#### Added 07/01/2015:

We will explore the outcome data to examine any relationship between the method of inclusion and compliance of the primary outcomes and if there is a difference in case mix, our modelled primary outcome analysis will adjust for this.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=14688

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

NRES committee North West - Preston, 03/05/2013, ref:13/NW/0279

## Study design

Cluster randomised controlled interventional trial

## Primary study design

Interventional

## Secondary study design

Cluster randomised trial

## Study setting(s)

Hospital

#### Study type(s)

Treatment

#### Participant information sheet

For this study we will not be actively recruiting patients as it is a retrospective notes review which is in a similar style to a robust clinical audit. Therefore there are no patient information sheets associated with this project.

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

Topic: Infection; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

#### Interventions

Package 1, there will be a series of interventions within the package that will be clinical led to help implement the national guidelines for management of suspected encephalitis patients.

#### **Intervention Type**

Other

#### Phase

Not Applicable

#### Primary outcome measure

Current primary outcome measures as of 07/01/2015:

The proportion of patients with suspected encephalitis whose care met all of the following criteria:

- 1. Aciclovir given within 6 hours of admission to hospital
- 2. A LP was performed within 12 hours of hospital arrival unless clinically contraindicated

Previous primary outcome measures:

The proportion of patients with suspected encephalitis whose care met all of the following criteria:

- 1. Aciclovir given within 6 hours of admission to hospital at the appropriate dose unless there was an alternative diagnosis
- 2. A LP was performed within 12 hours of hospital arrival unless clinically contraindicated.

#### Secondary outcome measures

Current secondary outcome measures as of 07/01/2015:

- 1. The proportion of all adults started on intravenous (IV) aciclovir within an appropriate dosage range for a neurological presentation who met the definition of suspected encephalitis
- 2. The proportion of all children started on intravenous (IV) aciclovir within an appropriate dosage range for a neurological presentation who met the definition of suspected encephalitis
- 3. The proportion of patients with suspected encephalitis who had a lumbar puncture performed within 12 hours unless there was a clinical contraindication
- 4. The proportion of patients with suspected encephalitis who had a lumbar puncture at any time within the index presentation
- 5. The proportion of patients with suspected encephalitis who had either MRI or CT scan within 24 hours of admission
- 6. The proportion of patients with suspected encephalitis having had a lumbar puncture, who had the following CSF investigations performed:
- 6.1. CSF:serum glucose ratio calculated
- 6.2. HSV PCR performed

- 7. An evaluation of the primary outcomes comparing adults and children enrolled in the RCT
- 8. A cost-effectiveness evaluation of the intervention

#### Previous secondary outcome measures:

- 1. The proportion of all adults given intravenous (IV) aciclovir for a neurological presentation who met the definition of suspected encephalitis.
- 2. The proportion of all children given IV aciclovir for a neurological presentation who met the definition of suspected encephalitis.
- 3. The proportion of patients with suspected encephalitis who had a lumbar puncture performed within 12 hours unless there was a clinical contraindication.
- 4. The proportion of patients with suspected encephalitis who had a lumbar puncture after resolution of a clinical contraindication to that LP.
- 5. The proportion of patients with suspected encephalitis who had either MRI or CT scan within 24 hours of admission.
- 6. For patients with HSV encephalitis, the proportion who die, have sequelae and appear to make a full recovery upon discharge.
- 7. The proportion of patients with suspected encephalitis having had a lumbar puncture, who had the following CSF investigations performed:
- 7.1. CSF:serum glucose ratio calculated
- 7.2. HSV PCR performed
- 8. An evaluation of the primary outcomes comparing adults and children enrolled in the RCT.
- 9. A cost-effectiveness evaluation of the intervention.

#### Overall study start date

20/01/2014

#### Completion date

15/07/2016

## **Eligibility**

#### Key inclusion criteria

Site inclusion criteria:

All centres will have a consultant and all centres must be equipped with the ability to perform, or have access to CT/MRI scans and have aseptic conditions for conducting a LP to be performed. Hospitals will be randomised as a unit to either the standard care or intervention arm. Study centres will be initiated once all global (e.g. local research and development [R&D] approval) and study-specific conditions (e.g. training requirements) have been met, and all necessary documents have been returned to the Brain Infections UK coordinating centre. Within this study, any patients who have suspected encephalitis within the recruited sites will be

Within this study, any patients who have suspected encephalitis within the recruited sites will be included in the study. The inclusion criteria for suspected encephalitis are:

#### Patients with suspected encephalitis

(a) Mandatory

Acute or sub-acute (<4 weeks) alteration in consciousness, cognition, personality or behaviour persisting for more than 24 hours. Personality/behaviour change includes: agitation, psychosis, somnolence, insomnia, catatonia, mood liability, altered sleep pattern and (in children): new onset enuresis, or irritability.

Plus ANY two of:

- 1. Fever (> 38°C) / prodromal illness acute or sub-acute
- 2. Seizures: new onset

- 3. Focal neurological signs acute or sub-acute onset. These include:
- 3.1. Focal weakness
- 3.2. Oromotor dysfunction
- 3.3. Movement disorders (chorea, athetosis, dystonia, hemiballisms, stereotypies, orolingual dyskinesia and tics) including Parkinsonism (bradykinesia, tremor, rigidity and postural instability)
- 3.4. Amnesia
- 4. Pleocytosis: cerebrospinal fluid white cell count >4 cells/ul
- 5. Neuroimaging: compatible with encephalitis
- 6. Electroencephalogram (EEG): compatible with encephalitis

OR

- (b) Clinical suspicion of encephalitis but above investigations have not yet been completed OR
- (c) Clinical suspicion of encephalitis and the patient died before investigations completed

Target Gender: Male & Female

#### Participant type(s)

**Patient** 

#### Age group

Adult

#### Sex

Both

#### Target number of participants

Planned Sample Size: Up to 1680; UK Sample Size: 1120 Up to 1680

#### Key exclusion criteria

Site exclusion criteria:

Current participation in the ENCEPH UK programme

#### Added 07/01/2015:

Patient exclusion criteria

Any patient aged under 28 days upon the date of admission shall be excluded

#### Date of first enrolment

03/02/2014

#### Date of final enrolment

31/05/2015

## Locations

#### Countries of recruitment

England

United Kingdom

Wales

## Study participating centre Blackpool Victoria Hospital

Blackpool United Kingdom FY3 8NR

## Study participating centre Queen Elizabeth Hospital

Gateshead United Kingdom NE9 6SX

## Study participating centre Queen Alexandra Hospital

Portsmouth United Kingdom PO6 3LY

## Study participating centre Doncaster Royal Infirmary

Doncaster United Kingdom DN2 5LT

## Study participating centre Stepping Hill Hospital

Stockport United Kingdom SK2 7JE

# Study participating centre Whiston Hospital

Prescot United Kingdom L35 5DR

## Study participating centre

## University Hospital Coventry and Warwick

Coventry United Kingdom CV2 2DX

## Study participating centre Addenbrooke's Hospital

Cambridge United Kingdom CB2 0QQ

## Study participating centre Countess of Chester Hospital

Chester United Kingdom CH2 1UL

## Study participating centre North Devon District Hospital

Devon United Kingdom EX31 4JB

## Study participating centre North Tees Hospital

Stockton-on-Tees United Kingdom TS19 8PE

## Study participating centre Bedford Hospital

Bedford United Kingdom MK42 9DJ

## Study participating centre

## Gloucestershire Royal Hospital

Gloucester United Kingdom GL1 3NN

## Study participating centre King's Mill Hospital

Sutton-in-Ashfield United Kingdom NG17 4JL

## Study participating centre Royal Sussex County Hospital

Brighton United Kingdom BN2 5BE

## Study participating centre Ormskirk and Southport Hospital

Ormskirk United Kingdom L39 2AZ

## Study participating centre West Suffolk Hospital

Bury St Edmunds United Kingdom IP33 2QZ

## Study participating centre Leicester Royal Infirmary

Leicester United Kingdom LE1 5WW

Study participating centre

## Russells Hall Hospital

Dudley United Kingdom DY1 2HQ

Study participating centre
Luton and Dunstable Hospital
Bedford
United Kingdom
LU4 0DZ

Study participating centre Great Western Hospital Swindon United Kingdom SN3 6BB

Study participating centre Ysbyty Gwynedd Gwynedd United Kingdom LL57 2PW

Study participating centre East Surrey Hospital Redhill United Kingdom RH1 5RH

Study participating centre Chesterfield Royal Hospital Chesterfield United Kingdom S44 5BL

## Sponsor information

#### Organisation

University of Liverpool (UK)

#### Sponsor details

University of Liverpool / Liverpool Joint Research Office 2nd Floor Block D Waterhouse Building 3 Brownlow Street Liverpool England United Kingdom L69 3GL

sponsor@liv.ac.uk

#### Sponsor type

University/education

#### Website

http://www.liv.ac.uk/

#### **ROR**

https://ror.org/04xs57h96

## Funder(s)

## Funder type

Government

#### **Funder Name**

National Institute for Health Research

## Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

## **Funding Body Type**

Government organisation

## Funding Body Subtype

National government

#### Location

**United Kingdom** 

## **Results and Publications**

## Publication and dissemination plan

The protocol is published and can be found at http://www.implementationscience.com/content /10/1/14. The paper describing the formation of the intervention package has been editorially accepted and we will publish the final trial results and a process evaluation at the end of data collection.

## Intention to publish date

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Other

## **Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	27/01/2015		Yes	No
Results article	results	01/12/2015		Yes	No
Results article	results	06/12/2018		Yes	No
HRA research summary			28/06/2023	No	No