

# Injury, inflammatory markers & the exacerbation of confusion: ASCRIBED

<b>Submission date</b> 21/11/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 11/05/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 03/10/2023	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Dementia is an umbrella term used to refer to a wide range of symptoms linked to with a reduction in memory and/or other thinking skills which reduce a person's ability to perform everyday activities. Inflammation is generally a beneficial response to tissue damage or infection. However, when inflammation is extensive or prolonged this can damage healthy tissues and disrupt normal cellular function. Research suggests that acute illnesses or injury causing inflammation can accelerate dementia. However there are few studies which examine underlying mechanisms of how this happens in humans. This study aims to address this gap. The study will compare markers of inflammation and injury found in the blood and cerebrospinal fluid (fluid which bathes the spinal cord (CSF)) of people with and without confirmed dementia who fracture their fracture. A hip fracture is a common example of an acute injury causing an inflammatory response. People who fracture their hip will undergo an operation to repair it. A common procedure during this operation is the giving of spinal aesthetic. This involves inserting a needle into the patient's spinal space and injecting anaesthesia into CSF. This means CSF can be collected before operation via the same needle.

### Who can participate?

Patients due to have a hip fracture operation via spinal anaesthesia with all levels of pre-operative confusion.

### What does the study involve?

Patients are allocated to one of three groups after their operation: those with confirmed dementia (as obtained from patient's GP notes/hospital records and/or carer insight), non-dementia (no evidence of dementia found in patient's GP notes/medical records) groupings; and pre-operatively confused but without confirmed dementia. Consent is gained for the storage of surplus samples in a bio-bank to help future studies. Pre-operative blood and CSF samples, post-operative blood samples and a short cognitive questionnaire is administered to all patients.

### What are the possible benefits and risks of participating?

For patients and their families there are no direct benefits taking part. However it is hoped that

the research may help similar patient groups in the future. Postdural-puncture headaches (PDPH) are a common side-effect of spinal anaesthesia. The collection of CSF may slightly increase the chance of PDPH.

Where is the study run from?

This study is being run by University of East Anglia (UK) and takes place in hospitals in the UK.

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

November 2016 to December 2022

Who is funding the study?

Alzheimer's Research UK (UK)

Who is the main contact?

Dr Simon Hammond

s.hammond@uea.ac.uk

## Contact information

**Type(s)**

Public

**Contact name**

Dr Simon Hammond

**ORCID ID**

<https://orcid.org/0000-0002-0473-3610>

**Contact details**

Norwich Medical School

University of East Anglia

Norwich Research Park

Norwich

United Kingdom

NR4 7TJ

+44 1603 591460

s.hammond@uea.ac.uk

## Additional identifiers

**Protocol serial number**

1

## Study information

**Scientific Title**

ASCRIBED: The impact of Acute Systematic inflammation upon cerebrospinal fluid and blood Biomarkers of brain inflammation and injury in Dementia: a study in acute hip fracture patients

**Acronym**

ASCRIBED

### **Study objectives**

The aim of this study is to evaluate whether hip fracture patients with dementia show elevated markers of systemic inflammation and of brain inflammation in comparison to stable patients with dementia and hip fracture patients without dementia, as measured by biomarkers in cerebrospinal fluid (CSF) and blood.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

NRES Committee North East - Newcastle & North Tyneside 1, 24/03/2017, ref: ISRCTN43803769

### **Primary study design**

Observational

### **Study design**

Observational case-control study

### **Study type(s)**

Other

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

Dementia patients admitted to acute hospital settings with a hip fracture.

### **Interventions**

Participants due to have a hip fracture operation via spinal anaesthesia with all levels of pre-operative confusion (as assessed by clinical screening procedures, AMTS (England) and 4AT (Scotland)) will be approached and recruited. Capacity will be assessed and consent or consultee agreement gained. During pre-operative procedures a blood sample will be taken and cerebrospinal fluid (CSF) collected.

48 hours post-operatively patients will be approached to undertake a short cognitive test and have a second blood sample collected. A suitable informant will also be sought to complete a proxy measure about the patient's memory and thinking. At 1 month post-operatively patient's GP and medical records will be accessed to search for evidence of dementia. Patients also taking part in ASCRIBED's sister study PERFECTED (ISRCTN99336264) will be asked to give blood samples at 1, 3 and 6 months post-operatively.

### **Intervention Type**

Other

### **Primary outcome(s)**

CSF inflammation and injury is measured by TNF- $\alpha$ , IL-1RA, IL-1 $\beta$ , IL-6 and Neurogranin, tTau, Synaptotagmin, SNAP-25 at baseline.

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

Magnitude of the brain inflammation is measured by brain injury markers (phospho-Tau, NFL, neurogranin, synaptotagmin, SNAP-25) in CSF at baseline.

### Exploratory:

1. Higher levels of inflammatory and brain injury markers in CSF and blood are associated with worsening cognitive and functional decline measured by MMSE at 6 months post-operatively
2. Cytokines ratio CSF: blood pre-op time will show higher ratios in dementia than non-dementia patients measures in blood and CSF at baseline

### Completion date

31/12/2022

## Eligibility

### Key inclusion criteria

Group 1: Pre-operative acute hip fracture patients with confusion as defined by the Abbreviated Mental Test (England) or 4AT (Scotland):

Inclusion Criteria:

1. Patient must have had a confirmed proximal hip fracture requiring an operation and be aged 60 or older at the time of operation
2. Patient has a pre-operative Abbreviated Mental Test score of 8 or below or 4AT score of 1 or above
3. Patient must be undergoing spinal anaesthesia

Group 2: Pre-operative acute hip fracture patients without confusion as defined by the Abbreviated Mental Test (England) or 4AT (Scotland):

Inclusion Criteria:

1. Patient must have had a confirmed proximal hip fracture requiring an operation and be aged 60 or older at the time of operation
2. Pre-operative Abbreviated Mental Test score of 9 or above or 4AT score of 0
3. Patient must be undergoing spinal anaesthesia

### Participant type(s)

Mixed

### Healthy volunteers allowed

No

### Age group

Adult

### Sex

All

### Total final enrolment

469

### Key exclusion criteria

Group 1 and 2:

1. Decision taken not to have hip surgery
2. Patient has head trauma with bleeding as indicated by a CT scan
3. Patient has confirmed diagnosis of Parkinson's disease
4. Patient not expected to survive beyond 4 weeks

**Date of first enrolment**

01/06/2017

**Date of final enrolment**

31/08/2019

## Locations

**Countries of recruitment**

United Kingdom

England

Scotland

**Study participating centre****Royal Infirmary of Edinburgh**

51 Little France Crescent

Edinburgh

United Kingdom

EH16 4SA

**Study participating centre****Leicester Royal Infirmary**

Infirmery Square

Leicester

United Kingdom

LE1 5WW

**Study participating centre****Royal Sussex County Hospital**

Eastern Road

Brighton

United Kingdom

BN2 5BE

**Study participating centre****Princess Royal University Hospital**

Farnborough Common

Orpington

United Kingdom

BR6 8ND

**Study participating centre**

**Royal Derby Hospital**

Uttoxeter Road  
Derby  
United Kingdom  
DE22 3NE

**Study participating centre**

**Pinderfields Hospital**

Mid Yorkshire Hospitals NHS Trust  
Wakefield  
United Kingdom  
WF1 4DG

**Study participating centre**

**York Teaching Hospital NHS Foundation Trust**

York  
United Kingdom  
YO31 8HE

**Study participating centre**

**Princess Royal Hospital**

Orpington  
United Kingdom  
BR6 8ND

**Study participating centre**

**James Paget University Hospital**

Great Yarmouth  
United Kingdom  
NR31 6LA

**Study participating centre**

**Russells Hall Hospital**

The Dudley Group NHS Foundation Trust  
Dudley  
United Kingdom  
DY1 2HQ

**Study participating centre**  
**Peterborough City Hospital**  
North West Anglia NHS Foundation Trust  
Peterborough  
United Kingdom  
PE3 9GZ

**Study participating centre**  
**Queen's Medical Centre Campus**  
Nottingham University Hospitals NHS Trust  
Nottingham  
United Kingdom  
NG7 2UH

**Study participating centre**  
**Royal Blackburn Hospital**  
East Lancashire Hospitals NHS Trust  
Blackburn  
United Kingdom  
BB2 3HH

**Study participating centre**  
**University Hospital of North Tees**  
North Tees and Hartlepool NHS Foundation Trust  
Stockton-on-Tees  
United Kingdom  
TS19 8PE

**Study participating centre**  
**The Royal Shrewsbury Hospital**  
The Shrewsbury and Telford Hospital NHS Trust  
Shrewsbury  
United Kingdom  
SY3 8XQ

**Study participating centre**  
**Doncaster Royal Infirmary**  
Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust  
Doncaster

United Kingdom  
DN2 5LT

**Study participating centre**

**Royal United Hospital Bath NHS Foundation Trust**  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**

**University Hospital of North Durham**  
County Durham and Darlington NHS Foundation Trust  
Durham  
United Kingdom  
DH1 5TW

**Study participating centre**

**Royal Bolton Hospital**  
Bolton NHS Foundation Trust  
Bolton  
United Kingdom  
BL4 0JR

**Study participating centre**

**Kingston Hospital**  
Kingston Hospital NHS Foundation Trust  
Kingston  
United Kingdom  
KT2 7QB

**Study participating centre**

**Royal Stoke University Hospital**  
University Hospitals of North Midlands NHS Trust  
Stoke-on-Trent  
United Kingdom  
ST4 6QG

**Study participating centre**

**Countess of Chester Hospital NHS Foundation Trust**  
Chester  
United Kingdom  
CH2 1UL

**Study participating centre**  
**Western Sussex Hospitals NHS Foundation Trust**  
-  
United Kingdom  
-

**Study participating centre**  
**Medway Maritime Hospital**  
Medway NHS Foundation Trust  
Gillingham  
United Kingdom  
ME7 5NY

**Study participating centre**  
**Whiston Hospital**  
St Helens & Knowsley Teaching Hospitals NHS Trust  
Rainhill  
United Kingdom  
L35 5DR

**Study participating centre**  
**Southampton General Hospital**  
University Hospital Southampton NHS Foundation Trust  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**  
**Royal Devon & Exeter Hospital**  
Royal Devon and Exeter NHS Foundation Trust  
Wonford  
United Kingdom  
EX2 5DW

**Study participating centre**

**Basildon University Hospital**

Basildon and Thurrock University Hospitals NHS Foundation Trust  
Basildon  
United Kingdom  
SS16 5NL

**Study participating centre**

**Musgrove Park Hospital**

Taunton and Somerset NHS Foundation Trust  
Taunton  
United Kingdom  
TA1 5DA

**Study participating centre**

**Scunthorpe General Hospital**

Northern Lincolnshire and Goole NHS Foundation Trust  
Scunthorpe  
United Kingdom  
DN15 7BH

**Study participating centre**

**Royal Lancaster Infirmary**

University Hospitals of Morecambe Bay NHS Trust  
Lancaster  
United Kingdom  
LA1 4RP

**Study participating centre**

**Yeovil District Hospital**

Yeovil District Hospital NHS Foundation Trust  
Yeovil  
United Kingdom  
BA21 4AT

**Study participating centre**

**Watford General Hospital**

West Hertfordshire Hospitals NHS Trust  
Watford  
United Kingdom  
WD18 0HB

**Study participating centre**  
**Sandwell General Hospital**  
Sandwell and West Birmingham Hospitals NHS Trust  
West Bromwich  
United Kingdom  
B71 4HJ

## Sponsor information

**Organisation**  
University of East Anglia

**ROR**  
<https://ror.org/026k5mg93>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Alzheimer's Research UK

**Alternative Name(s)**  
Alzheimer's Research Trust, AlzResearchUK, AlzheimersResearch UK, ARUK

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Trusts, charities, foundations (both public and private)

**Location**  
United Kingdom

## Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof Chris Fox, Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, United Kingdom.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	07/09/2019	09/12/2020	Yes	No