

A study comparing pre-hospital administration of packed red blood cells and freeze-dried plasma with administration of normal saline in patients with low blood pressure after major injuries

Submission date 11/07/2016	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 11/07/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 02/09/2024	Condition category Injury, Occupational Diseases, Poisoning	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Major trauma accounts for a significant number of deaths worldwide, and is one of the most frequent causes of death in people under the age of 40. A large number of these deaths are caused by major bleeding as a result of the trauma (traumatic haemorrhage). Patients with traumatic haemorrhage are currently given clear fluids but military and civilian research suggests that survival increases if hospital patients receive blood products (red blood cells and freeze-dried plasma) instead. The best treatment for bleeding patients before reaching hospital is uncertain. Giving too much fluid to improve blood pressure can increase bleeding. Therefore only small amounts of clear fluid are given. Some pre-hospital doctors now give red blood cells instead. Animal research suggests that this is better than clear fluids, and that adding plasma is better still. Some studies in humans support this however other research has found no benefit. There is currently no good quality evidence exists to show whether giving blood products before hospital, saves lives. The aim of this study is to find out whether giving blood products to badly injured adult patients, before reaching hospital improves their clinical condition and survival.

Who can participate?

Patients believed to be over the age of 16 who have sustained a serious injury leading to major blood loss.

What does the study involve?

Participants are randomly allocated to one of two groups at the scene of the emergency. Those in the first group receive fluids through a drip, with up to four bags of normal saline (salt water). Those in the second group receive two units of concentrated red blood cells and two units of freeze dried plasma (straw like fluid that makes up the liquid part of blood). Participants in both groups are followed up for 30 days to find out if any patients died (of their injuries or otherwise), as well as the speed they are able to clear lactic acid from their tissues (indicator of good blood

flow). Blood pressure, heart rate, blood clotting and whether patients need organ support are also monitored while they are on intensive care.

What are the possible benefits and risks of participating?

There are no guaranteed direct benefits involved with participating in this study however the blood product treatment could be shown to be more effective than standard treatment. There are no notable risks involved for those participating in this study.

Where is the study run from?

Pre-hospital emergency medicine and major trauma centres in the West Midlands, Dorset & Somerset and in the East of England (UK)

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

October 2015 to April 2020

Who is funding the study?

National Institute for Health Research (UK)

Who is the main contact?

Miss Gemma Slinn, rephill@trials.bham.ac.uk

Study website

<https://www.birmingham.ac.uk/rephill>

Contact information

Type(s)

Public

Contact name

Miss Gemma Slinn

Contact details

Birmingham Clinical Trials Unit

University of Birmingham

Birmingham

United Kingdom

B15 2TT

+44 121 415 9100

rephill@trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number

2015-001401-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

31157

Study information

Scientific Title

A multi-centre randomised controlled trial of pre-hospital blood product administration versus standard care for traumatic haemorrhage

Acronym

RePHILL

Study objectives

The aim of this study is to investigate whether giving blood products (red blood cells and freeze-dried plasma) to badly injured adult patients, before reaching hospital improves their clinical condition and survival.

Ethics approval required

Old ethics approval format

Ethics approval(s)

South Central - Oxford C Research Ethics Committee, 15/12/2015, ref: 15/SC/0691

Study design

Randomised; Interventional; Design type: Treatment, Drug

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Traumatic haemorrhage

Interventions

Participants are randomised in a 1:1 ratio to receive:

Crystalloid resuscitation: Consisting of up to 4 x 250 mL bags of 0.9% sodium chloride (normal saline). These will be administered as boluses of 250 mL to maintain a radial pulse

Pre-Hospital Blood Products (BHBP) resuscitation: Consisting of up to 2 units of PRBC and 2 units of LyoPlas. These will be administered as boluses consisting of a single unit of blood product, given in the sequence: PHBP, LyoPlas, PHBP, LyoPlas.

LyoPlas N-w is a freeze dried plasma product derived from a single donation and is licenced for use in the same indication as fresh frozen plasma. LyoPlas N-w is licensed for use in Germany as a medicinal product under the Marketing Authorisation Number PEI.H.03075.01.1.

PRBC are a concentrated preparation of red blood cells that is obtained from whole blood by removing the plasma (as by centrifugation). The PRBC used in RePHILL will be blood group O, RhD negative, Kell negative from NHS Blood and Transplant national stocks supplied by the blood banks that are supporting this trial.

Patients receive the trial interventions on-scene, because of the emergency nature of this trial, patients are considered randomised when the transport box containing the interventions is opened. Follow-up will comprise of standard care follow-up for patients that have a traumatic injury, no further trial-specific procedures will be undertaken after the delivery of the interventions but we will collect data pertaining to the RePHILL outcome measures for up to 30 days post-injury.

Intervention Type

Other

Phase

Phase III

Primary outcome measure

1. Episode mortality is measured by whether or not the patient is still alive up to 30 days post injury up to 30 days post injury
2. Lactate clearance is measured by obtaining a lactate measurement at randomisation and a repeat measurement two hours post-randomisation

Secondary outcome measures

1. All-cause mortality rate is measured by whether or not the patient is still alive within 3 hours of randomisation
2. Pre-hospital time and type and volume of fluid is measured by the pre-hospital emergency medical team at on-scene.
3. Vital signs (systolic blood pressure, heart rate, capillary oxygen saturation) are measured at scene, on arrival at ED and at 2, 6, 12 and 24 hours after arrival at ED
4. Venous lactate concentration is measured by the receiving hospital medical team on arrival at ED and at 2 hours after arrival at ED
5. Trauma-induced coagulopathy (defined as International Normalised Ratio (INR) >1.5) is measured by measuring clotting factors on arrival at ED and at 2 and 6 hours after arrival at ED
6. Coagulation is measured using viscoelastically by rotational thromboelastometry on arrival at ED
7. Platelet function is measured using multiple electrode impedance aggregometry on arrival at ED
8. Total blood product receipt is measured by recording fluids given to the patient at 6, 12 and 24 hours after arrival at ED
9. Acute respiratory distress syndrome (ARDS) is measured by the presence of clinical symptoms within the first 7 days after injury
10. Transfusion-related complications are measured by the presence of clinical symptoms up to 30 days post injury

11. Organ failure-free days are measured using the Sepsis-related Organ Failure Assessment (SOFA) score up to 30 days post injury

Overall study start date

01/10/2015

Completion date

31/05/2021

Eligibility

Key inclusion criteria

1. Traumatic injury
2. Pre-Hospital Emergency Medical team attend
3. Hypotension (SBP <90mmHg or absence of palpable radial pulse) believed to be due to traumatic haemorrhage

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

Planned Sample Size: 490; UK Sample Size: 490

Total final enrolment

432

Key exclusion criteria

1. Children (known or apparently aged <16 years)
2. Refusal of blood product administration; known Jehovah's Witness
3. Pregnancy (known or apparent)
4. Isolated head injury

Date of first enrolment

01/10/2016

Date of final enrolment

31/12/2020

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

University Hospitals Birmingham NHS Foundation Trust

Queen Elizabeth Hospital
Mindelsohn Way
Birmingham
United Kingdom
B15 2WB

Study participating centre

West Midlands Ambulance Service NHS Foundation Trust

Trust Headquarters
Millennium Point
Waterfront Business Park
Waterfront Way
Brierley Hill
United Kingdom
DY5 1LX

Study participating centre

West Midlands Air Ambulance/ MERIT

Midlands Air Ambulance Charity
Hawthorn House
Dudley Road
Stourbridge
United Kingdom
DY9 8BQ

Study participating centre

Warwickshire and Northamptonshire Air Ambulance

The Air Ambulance Service
Hazell House
Burnthurst Lane
Princethorpe
United Kingdom
CV23 9QA

Study participating centre

Yorkshire Ambulance Service

Headquarters, Springhill
Brindley Way
Wakefield 41 Business Park

Wakefield
United Kingdom
WF2 0XQ

Study participating centre

Yorkshire Air Ambulance

Cayley House
10 South Lane
Elland
United Kingdom
HX5 0HQ

Study participating centre

East of England Ambulance Service NHS Trust

East of England Ambulance Service NHS Trust Headquarters
Whiting Way
Melbourn
Melbourn
United Kingdom
SG8 6EN

Study participating centre

MAGPAS

Centenary House
St. Mary's Street
Huntingdon
United Kingdom
PE29 3PE

Study participating centre

East Anglian Air Ambulance

Hangar E
Gambling Close
Norwich Airport
Norwich
United Kingdom
NR6 6EG

Study participating centre

Essex & Herts Air Ambulance

Essex and Herts Air Ambulance Trust

Flight House
Earls Colne Business Centre
Earls Colne Business Park
Earls Colne
Colchester
United Kingdom
CO6 2NS

Study participating centre
East Midlands Ambulance Service NHS Trust
Trust Headquarters
1 Horizon Place
Mellors Way
Nottingham Business Park
Nottingham
United Kingdom
NG8 6PY

Study participating centre
Derbyshire, Leicestershire and Rutland Air Ambulance
35 King Street
Belper
United Kingdom
DE56 1PX

Study participating centre
Warwickshire and Northamptonshire Air Ambulance
The Air Ambulance Service
Hazell House
Burnthurst Lane
Princethorpe
United Kingdom
CV23 9QA

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
University Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre

University Hospitals of North Midlands NHS Trust

Royal Stoke University Hospital

Newcastle Road

Stoke-on-Trent

United Kingdom

ST4 6QG

Study participating centre

North Bristol NHS Foundation Trust

Southmead Hospital

Southmead Road

Westbury-on-Trym

Bristol

United Kingdom

BS10 5NB

Study participating centre

The Leeds Teaching Hospital NHS Trust

Leeds General Infirmary

Great George Street

Leeds

United Kingdom

LS1 3EX

Study participating centre

South Tees Hospital NHS Foundation Trust

James Cook Hospital

Marton Road

Middlesbrough

United Kingdom

TS4 3BW

Study participating centre

Hull and East Yorkshire Hospitals NHS Trust

Hull Royal Infirmary

Anlaby Road

Hull

United Kingdom

HU3 2JZ

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

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Addenbrooke's Hospital
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Norfolk & Norwich University Hospitals NHS Foundation Trust
Norfolk and Norwich University Hospital
Colney Lane
Norwich
United Kingdom
NR4 7UY

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

Sponsor information

Organisation
University Hospitals Birmingham NHS Foundation Trust

Sponsor details
Trust HQ
PO BOX 9551

Queen Elizabeth Medical Centre
Edgbaston
Birmingham
England
United Kingdom
B15 2TH

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/014ja3n03>

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

Current participant exclusion criteria as of 06/03/2020:

The main trial results will be submitted for publication in a high-impact peer-reviewed journal.

The trial protocol will be published in October 2018.

Intention to publish date

31/05/2022

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are not expected to be made available

Previous participant exclusion criteria:
Planned publication in a high-impact peer reviewed journal. A protocol paper will be published within the next six months.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/10/2018	06/03/2020	Yes	No
Results article		04/03/2022	11/03/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/01/2024	02/09/2024	Yes	No