ISRCTN28818784 https://doi.org/10.1186/ISRCTN28818784

A randomised trial to investigate whether giving more blood transfusions to people undergoing surgery for hip fracture improves their outcomes

Submission date
28/04/2022

Recruitment status
Recruiting

Registration date
03/05/2022

Overall study status
Ongoing

Last Edited
25/07/2024

Condition category
Surgery

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English Summary
Background and study aims
Hip fracture is the most common serious injury in older people. More than 95% of patients have surgery. This surgery is often high-risk as patients may be frail and have other health problems including heart disease and anaemia (a low blood count). Patients may be in hospital for a long time and need rehabilitation. Up to 35% of surviving patients do not return to their original residence and have a high rate of increased dependency.
Research suggests that 30-40% of these patients have a blood transfusion around the time of operation. However, doctors are uncertain about what level of anaemia transfusions should be given at. Many current guidelines recommend transfusion at a lower level, but there is research which suggests that this level is too low particularly if the patient has a history of heart disease. In these patients, transfusion at a higher level may be better to prevent complications.

Who can participate?
Older (60 years or older) people with a hip fracture and anaemia

What does the study involve?
Participants will be randomly assigned to either receive blood transfusions at a lower blood count, in line with current guidelines, or a higher level, for the duration of their hospital stay, or 30 days, whichever is soonest.
Patients will have their blood count checked before and after any blood transfusions and will have additional blood tests (Troponin) and heart tracings (electrocardiographs, (ECG)) to check their heart.
At 30 days we will measure how often post-operative heart attacks and other complications occur, how long patients stay in hospital and mortality rate. At 30 and 120 days we will measure quality of life (assessed by questionnaire).
The study will last for 4 years but each patient will only be active in the study for 120 days. The study results will help doctors looking after people with hip fracture decide when is the best time to give blood transfusions

What are the possible benefits and risks of participating?
Benefits: There are no clear benefits of taking part in the study. Participants in the liberal arm of the study may receive a few additional transfusions than they would have had if they had not participated in the trial and participants in the restrictive arm may receive slightly fewer transfusions. One arm may be beneficial to participants but we do not know which and are conducting the study to try and find out.

Risks: Blood transfusions are generally very safe but they do carry risks. Transfusion reactions can occur but these are rare and usually mild (for example a fever or rash). Transfusions also have an increased risk of infections or pulmonary oedema although these are very rare.

Where is the study run from?
University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
August 2021 to April 2027

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Prof. Michael Gillies, michael.gillies@nhslothian.scot.nhs.uk

Study website
https://www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies/all-current-studies/result-hip

Contact information

Type(s)
Scientific

Contact name
Prof Michael Gillies

ORCID ID
http://orcid.org/0000-0003-1909-0790

Contact details
The University of Edinburgh
Dept of Anaesthesia, Critical Care and Pain Medicine
Royal Infirmary of Edinburgh
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United Kingdom
EH16 4SA
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michael.gillies@nhslothian.scot.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
308830, 299977

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 52646, IRAS 299977 (Scotland), IRAS 308830 (England and Wales), AC21119

Study information

Scientific Title
The impact of REStrictive versUs Liberal Transfusion strategy on cardiac injury and death in patients undergoing surgery for Hip Fracture (RESULT-Hip)

Acronym
RESULT Hip Version 1

Study hypothesis
Do patients with hip fracture have better clinical outcomes when a more liberal transfusion practice is used to treatanaemia?

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 17/03/2022, Scotland A Research Ethics Committee (2ndFloor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, UK; +44 (0)7814 764 241; manx.neill@nhslothian.scot.nhs.uk), ref: 22/SS/0001
2. Approved 18/03/2022, North West- Haydock Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 207 1048032; haydock@rec.hra.nhs.uk), ref: 22/NW/0065

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Patient information material can be found at https://www.ed.ac.uk/usher/edinburgh-clinical-trials/our-studies/all-current-studies/result-hip/result-hip-study/about-study

Condition

Blood transfusion for recovery from hip surgery

Interventions

Current interventions as of 17/11/2023:
RESULT-Hip is a multicentre randomised trial of the effect of two blood transfusion strategies in patients with hip fractures on cardiac complications. One group of patients will have a restrictive transfusion strategy, which follows published guidelines, and the other a more liberal strategy. This is described more fully below. The study will take place in 30 UK hospitals that look after patients with hip fractures.

When a patient is admitted to the hospital after breaking their hip, almost all go on to have surgery to treat this condition. They will be assessed by the clinical team or research team (where part of the clinical team) in the hospital to see if they meet the age inclusion criteria and do not have any exclusion criteria for the study. Those receiving palliative care (i.e. do not have surgery), who have life-threatening haemorrhage at the time of screening, pre-randomisation acute, or suspected acute, coronary syndrome, objection to receiving RBC transfusion or chronic transfusion-dependent anaemia, will be excluded. This can take place from the time the patient enters the hospital and up to and including 7 days post-surgery.

If the patient meets the criteria they will be approached by a member of the clinical team or research team (where part of the clinical team) to discuss whether they are interested in taking part in the study. If they are, a member of the research team will take consent from the patient to randomise them to the study if they become anaemic (Hb ≤90 g/L) (considered 'consent in principle' or pre-consent')

If the patient lacks mental capacity, then the research team will approach a family member or personal consultee, or professional consultee (if appropriate) to discuss the patient taking part in the study.

If the patient (or consultee) consents then if the Hb trigger value (Hb ≤90 g/L) is reached the patient will be randomised to one arm or other of the study. The two arms will have all the same tests done. The difference between the two will be the point at which a blood transfusion is given.

In one arm the transfusion will be given when the level of haemoglobin in the blood is ≤ 90g/L. This is called the “liberal” transfusion strategy. The aim will be to keep the haemoglobin in the range 90 - 110g/L. In the other arm the transfusion will be given when the level of haemoglobin in the blood is ≤ 75g/L. This is called the “restrictive” transfusion strategy and is the usual, or standard, level of transfusion in patients undergoing surgery for hip fracture.
The aim will be to keep the haemoglobin in the range 75-90 g/L. Participants in both arms of the trial will follow either the restrictive or liberal strategy for the duration of their stay in acute hospital or until 30 days following randomisation whichever is soonest.

We will follow up what happens to all the patients on both arms. The main (primary) outcome (we are interested in studying is about damage to the heart (cardiac injury) and death after this emergency surgery. The rate of occurrence of each of these may be different in the two arms of the study.

To accurately measure the rate of damage to the heart, participants in both arms of the trial will have some additional tests done specifically for the study. They will have blood samples taken to check for levels of a chemical called troponin. Blood samples for troponin testing will be taken when participants are randomised to the trial and twice more between days 1 and 5 following randomisation. Where possible blood samples will be taken at the same time as routine hospital blood samples to minimise inconvenience to the participant. The blood samples will be frozen at the hospital and later transported to Edinburgh for analysis.

Participants will have electrocardiographs (ECG, or heart trace) taken at randomisation and once more during days 2-5 following randomisation. The ECG checks the heart's rhythm and electrical activity. It is a common and painless test carried out by attaching sensors to the participant's chest.

We are also interested in how the participant's quality of life is affected by the intervention, and we will ask them to complete a simple quality of life questionnaire (EQ-5D-5L), which takes just a few minutes to complete, at the time they are randomised to the study.

We will collect data at 30 days and 120 days after randomisation if the participant is still alive. This will allow us to assess whether the blood transfusion affects time in hospital, recovery, and quality of life after this type of surgery. This will be done by asking the participant to complete the EQ-5D-5L questionnaire again which can be done over the telephone. We will also ask the participant to answer a short questionnaire about their health service usage at both 30 and 120 days. The rest of the data that we need for the study is collected from the participant's medical records. After these final questionnaires, at 120 days, we will not require anything else from the participant.

In participants that lack capacity, we will ask the participant's personal consultee to complete the proxy EQ-5D-5L questionnaire at randomisation. We will ask the consultee for permission to contact them at 30 and 120 days (if the participant has not regained capacity) for the completion of the EQ-5D-5L and health resource questionnaires on the participant's behalf.

To answer the study question accurately we will need to recruit 1964 patients, they will be split between the two arms of the study. This will allow us to detect a difference in the main outcome. This figure has been calculated using information from our previous pilot study and allows for some patients to drop out of the study.

The whole project will take 48 months to complete. However, each patient is only actively involved for 120 days post-randomisation.

Process Evaluation
We will include a process evaluation of the internal pilot study consistent with MRC guidance. Our objectives are: to establish the extent to which the intervention is implemented as intended during the internal pilot across different sites; to ascertain how feasible and acceptable the intervention is to clinical staff across different sites; to identify any facilitators and barriers to recruitment.

The methods used to conduct the PE of the internal pilot will be: During Site Initiation Visit - to identify key research staff, collect baseline data on context and establish the acceptability of study protocol. During the internal pilot - all sites in the internal pilot will be invited to participate in individual interviews. Interviews will be conducted remotely by telephone, or by web-based service. Sampling will be used to ensure a range of participants according to grade, profession and role in the research or clinical teams. Interviews will be recorded, transcribed and analysed to identify common themes. The findings of the process evaluation will be reported to the Trial Management and Trial Steering Groups and will feed into decisions about the on-going progress and management of the trial.

Previous interventions:
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Intervention Type
Other

Primary outcome measure
Death or major cardiac adverse events (MACE) measured using patient records up to 30 days

Secondary outcome measures
Measured using patient records at 30 days:
1. All cause mortality
2. Myocardial injury post randomisation (troponin >99th centile (URL) AND a 20% change from baseline)
3. Individual MACE components
4. Complications (including AKI, delirium, stroke, pulmonary embolus)
5. Proportion of participants transfused
6. Discharge destination
7. Acute hospital length of stay
8. EQ-5D-5L9. Health services resource utilisation (from questionnaires)

Additional secondary outcome measures
Measured using patient records at 120 days:
1. All cause mortality
2. Discharge destination
3. Acute hospital length of stay
4. unplanned hospital readmissions
5. Mobility
6. Residential status
7. EQ-5D-5L9., Health services resource utilisation (from questionnaire)

Overall study start date
01/08/2021

Overall study end date
30/04/2027

Eligibility

Participant inclusion criteria
Current participant inclusion criteria as of 17/11/2023:
1. Adults aged 60 years or over
2. Admission to acute unit for operative management of hip fracture

For Randomisation:
3. Presence of anaemia (Haemoglobin equal to or less than 90 g/L) at any point between the date of admission to hospital up to and including seven days after surgery

Previous participant inclusion criteria:
1. Adults aged 60 years or over
2. Admission to hospital for operative management of hip fracture

For Randomisation:
3. Presence of anaemia (Haemoglobin equal to or less than 90 g/L) at any point between the date of admission to hospital up to and including seven days after surgery

Participant type(s)
Patient

Age group
Adult

Lower age limit
60 Years

Sex
Both

Target number of participants
Planned Sample Size: 1964; UK Sample Size: 1964

Participant exclusion criteria
Current participant inclusion criteria as of 17/11/2023:
1. Objection to RBC transfusion
2. Unable to obtain consent (from patient or in accordance with appropriate mental capacity legislation for site)
3. Patients for non-operative management or not expected to survive 48 hours
4. Patients with a new or suspected acute coronary syndrome meeting 4th Universal Definition during current admission
5. Rapid or uncontrolled blood loss resulting in haemodynamic instability
6. Transfusion dependent/chronic anaemias (eg Myelodysplasia or bone marrow failure syndromes)

Previous participant inclusion criteria:
1. Objection to RBC transfusion
2. Unable to obtain consent (from patient or in accordance with appropriate mental capacity legislation for site)
3. Patients for non-operative management or not expected to survive 48 hours
4. Patients with a new acute coronary syndrome meeting 4th Universal Definition during current admission
5. Rapid or uncontrolled blood loss resulting in haemodynamic instability

Recruitment start date
01/06/2022

Recruitment end date
30/04/2026

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
United Kingdom
G4 0SF

Study participating centre
Wishaw General Hospital
50 Netherton Street
Wishaw
United Kingdom
ML2 0DP

Study participating centre
Borders General Hospital
Huntlyburn Terrace
Melrose
United Kingdom
TD6 9BS

Study participating centre
Rotherham General Hospital
Moorgate Road
Rotherham
United Kingdom
S60 2UD

Study participating centre
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol
United Kingdom
BS10 5NB

Study participating centre
Norfolk and Norwich University Hospital
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre

Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
United Kingdom
TS19 8PE

Study participating centre
Dumfries and Galloway Royal Infirmary
Bankend Road
Dumfries
Dumfries and Galloway
United Kingdom
DG1 4AP

Study participating centre
Victoria Hospital
Hayfield Road
Kirkcaldy
United Kingdom
KY25AH

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Horton General Hospital
81a Oxford Road
Banbury
United Kingdom
OX16 9AL

Study participating centre
Hereford County Hospital
Stonebow Road
Hereford
United Kingdom
HR1 2BN

Study participating centre
Royal Albert Edward Infirmary
Wigan Lane
Wigan
United Kingdom
WN1 2NN

Study participating centre
Ipswich Hospital
Heath Road
Ipswich
United Kingdom
IP4 5PD

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

Study participating centre
Worcestershire Royal Hospital
Charles Hastings Way
Worcester
United Kingdom
WR5 1DD

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road

Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
North Devon District Hospital
Raleigh Park
Barnstaple
United Kingdom
EX31 4JB

Study participating centre
Darlington Memorial Hospital
Hollyhurst Road
Darlington
United Kingdom
DL3 6HX

Study participating centre
Royal Devon and Exeter Hospital
Royal Devon & Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
University Hospital of North Durham Cdc
University Hospital of North Durham
North Road
Durham
United Kingdom
DH1 5TW

Study participating centre
Southport and Formby District General Hospital
Town Lane
Southport
United Kingdom
PR8 6PN

Study participating centre
Stoke Mandeville Hospital
Mandeville Road
Aylesbury
United Kingdom
HP21 8AL

Study participating centre
Royal Victoria Hospital
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Sponsor information

Organisation
University of Edinburgh and NHS Lothian Health Board

Sponsor details
The University of Edinburgh
Usher Building
5-7 Little France Road
Edinburgh Bioquarter Gate 3
Edinburgh
Scotland
United Kingdom
EH6 4UX
+44 131 2423326
resgov@accord.scot

Sponsor type
University/education

Website
https://www.accord.ed.ac.uk

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

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
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
30/06/2027

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be 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?
HRA research summary			28/06/2023	No	No
HRA research summary			26/07/2023	No	No
Protocol file	version 3	15/09/2022	17/11/2023	No	No
Protocol file	version 4	03/05/2023	25/07/2024	No	No