# A multi centre randomised controlled trial comparing intra operative cell salvage with standard care in the treatment of hip fractures

<b>Submission date</b> 27/08/2019	Recruitment status  No longer recruiting	[X] Prospectively registered
		[X] Protocol
Registration date	Overall study status	Statistical analysis plan
10/09/2019	Completed	☐ Results
Last Edited	Condition category	Individual participant data
09/06/2022	Injury, Occupational Diseases, Poisoning	<ul><li>Record updated in last year</li></ul>

#### Plain English summary of protocol

Current plain English summary as of 08/04/2020:

#### Background and study aims

Patients admitted with a hip fracture are typically elderly, frail and have multiple medical comorbidities, including low red bold cell count (anaemia). As a consequence of the fracture and urgent surgery, patients sustain blood loss, worsening this pre-existing anaemia. In patients with a fractured hip allogenic (blood from a donor) blood transfusion is required in up to 30% of patients. Blood transfusions impose some risks to patients, such as an increased rate of infection. Allogenic blood use is associated with transfusion reactions and an increased length of hospital stay. Concerns regarding patient safety and the costs of allogenic blood have driven efforts to reduce transfusion rates. 'Intraoperative cell salvage and autotransfusion' is a method of collecting blood lost during surgery and transfusing it back to the patient. The cell salvage device separates oxygen-carrying red blood cells lost during surgery, prior to transfusing them back to the patient. Complications as a result of cell salvage are rare. Despite not currently being used routinely, there are large potential benefits of using cell salvage during hip fracture surgery. The study aim is to evaluate the clinical effectiveness of cell salvage in hip fracture surgery.

#### Who can participate?

Participants of 60 years of age and older who have sustained a fracture of the hip who, in the opinion of the operating surgeon, would benefit from surgery

#### What does the study involve?

The study will include a comparison between 'cell salvage' with 'treatment as usual' to the blood lost during hip surgery. Treatment as usual involves a standard suction system removing blood lost in the operation and disposed of in clinical waste. In either treatment arm patients may receive donor's blood transfusion before the operation. Then need for allogenic blood products will be determined on an individual patient basis, following each centres blood transfusion policy.

What are the possible benefits and risks of participating?

Any operation for a broken hip carries some risks. The risk of surgery with an implant include: bleeding requiring blood transfusion, infection, further fracture, dislocation, leg length discrepancy, blood clots, damage to nerves and blood vessels in the surgical care, and the risks associated with the anaesthetic. Allogenic blood transfusion carries the risk of increased rate of local and systematic infections. These risks are the same as for patients who are not part of this research project. Cell salvage is very safe as patients own blood is used. There is no specific advantage for participant taking part in the trials. However, the information we get from this trial will inform the future practice and will benefit future patients.

Where is the study run from?

John Radcliffe Hospital, Oxford, UK

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

Who is funding the study? National Institute for Health Research (NIHR)

Who is the main contact? Katy Mironov White9@ndorms.ox.ac.uk

Previous plain English summary:

Background and study aims

Patients admitted with a hip fracture are typically elderly, frail and have multiple medical comorbidities, including low red bold cell count (anaemia). As a consequence of the fracture and urgent surgery, patients sustain blood loss, worsening this pre-existing anaemia. In patients with a fractured hip allogenic (blood from a donor) blood transfusion is required in up to 30% of patients. Blood transfusions impose some risks to patients, such as an increased rate of infection. Allogenic blood use is associated with transfusion reactions and an increased length of hospital stay. Concerns regarding patient safety and the costs of allogenic blood have driven efforts to reduce transfusion rates. 'Intraoperative cell salvage and autotransfusion' is a method of collecting blood lost during surgery and transfusing it back to the patient. The cell salvage device separates oxygen-carrying red blood cells lost during surgery, prior to transfusing them back to the patient. Complications as a result of cell salvage are rare. Despite not currently being used routinely, there are large potential benefits of using cell salvage during hip fracture surgery.

The study aim is to evaluate the clinical effectiveness of cell salvage in hip fracture surgery. Prior to assessing this in a full-size clinical trial we need to understand if surgeons and patients are willing to participate in such a study and if sufficient blood is lost during surgery to make cell salvage viable. Therefore this is a feasibility study to determine if a full study is possible and worthwhile.

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Where is the study run from? John Radcliffe Hospital, Oxford, UK

When is the study starting and how long is it expected to run for? October 2019 to September 2020

Who is funding the study?
National Institute for Health Research (NIHR)

Who is the main contact? Katy Mironov White9@ndorms.ox.ac.uk

# **Contact information**

Type(s)

Scientific

#### Contact name

Mrs Katy Mironov

#### Contact details

Oxford Trauma Kadoorie Centre Level 3 John Radcliffe Hospital Headley Way Oxford United Kingdom OX3 9DU +44 (0)1865 227226 White9@ndorms.ox.ac.uk

# Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

#### ClinicalTrials.gov (NCT)

Nil known

#### Protocol serial number

**CPMS 42503** 

# Study information

#### Scientific Title

The World Hip Trauma Evaluation Nine (WHiTE 9) BeST: A multi-centre randomised controlled trial comparing intraoperative cell salvage with standard care in the treatment of hip fractures

#### **Acronym**

WHITE 9

#### **Study objectives**

The aim of the main study is to determine the clinical and cost-effectiveness of intraoperative cell salvage, compared to standard care, in improving health-related quality-of-life in patients undergoing hip fracture surgery.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

- 1. Approved 14/08/2019, Wales Research Ethics Committee 5 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB; +447970422139; Wales. REC5@wales.nhs.uk), ref: 19/WA/0197
- 2. Amendment 02 for the main study approved by Wales Research Ethics Committee 5 on 03/04/2020 (details as above)

#### Study design

Randomised; Interventional; Design type: Treatment, Surgery

# Primary study design

Interventional

#### Study type(s)

Treatment

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

Fracture of neck of femur

#### **Interventions**

Current interventions as of 08/04/2020:

Patients over 60 years of age, both those with and without capacity, who sustain a hip fracture and are treated operatively, will be potentially eligible to be randomised to either undergo cell salvage or they will follow the standard care pathway- a standard suction system removes blood lost in the operating field and it is disposed of in the clinical waste.

In either treatment arm, patients may receive donor's (allogenic) blood transfusion before the operation. The need for allogenic blood products will be determined on an individual patient basis, following each centre's blood transfusion policy.

Patients who are younger than 60, treated non-operatively or undergoing cannulated hip screw fixation will not be eligible. Patients for whom the treating surgeon has already elected to use cell salvage (for example Jehovah Witness) or those who have sustained a pathological fracture will also be excluded.

Participants will undergo surgery at the next available opportunity on a planned trauma list. Participants will be blinded to the treatment allocation. The operating surgeon cannot be blinded to the allocation but they will not be involved in the assessment of outcomes. Participants will be kept blinded until the completion of the trial when the blinding will be broken if requested by the patients. There will be no formal analysis of the success of the blinding.

Following hip surgery, all patients will undergo a routine rehabilitation prior to discharge from the hospital. Research staff will complete the data regarding the operation received and autotransfusion blood volume will be recorded at baseline. In addition, the following data will be collected:

- Demographic and baseline characteristics (e.g. age, gender, pre-fracture mobility)
- Pre-injury quality of life (EQ5D) and at 4 and 12 months postoperatively
- Routine 'operation notes', perioperative complications, and discharge details
- The volume of blood that was autotransfused, when this was possible
- The number of donor blood units transfused and the date of transfusion will be collected
- Haemoglobin concentration
- Pre and postoperative delirium assessment
- Details of admission, assessment and treatment
- Contact details, including of carers when appropriate
- Complications and SAEs during the study period

Following their 12 months questionnaire, patients will have completed their participation in the trial and will continue to be treated as per normal standard of care.

#### Previous interventions:

This will be a multi-centre feasibility randomised controlled trial. The study will include a comparison between a cell salvage and autotransfusion with the standard of care approach to the blood lost during hip surgery. The study will be linked to the established WHiTE Comprehensive Cohort Study.

Patients over 60 years of age, both those with and without capacity, who sustain a hip fracture and are treated operatively, will be potentially eligible to be randomised to either undergo cell salvage and autotransfusion or they will follow the standard care pathway- a standard suction system removes blood lost in the operating field and it is disposed of in clinical waste. In either treatment arm, patients may receive donor's (allogenic) blood transfusion before the operation. The need for allogenic blood products will be determined on an individual patient basis, following each centre's blood transfusion policy.

Patients who are younger than 60, treated non-operatively or undergoing cannulated hip screw fixation will not be eligible. Patients for whom the treating surgeon has already elected to use cell salvage (for example Jehovah Witness) or those who have sustained a pathological fracture will also be excluded.

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Following hip surgery, all patients will undergo a routine rehabilitation prior to discharge from the hospital. Research staff will complete the data regarding the operation received and autotransfusion blood volume will be recorded at baseline. In addition, the following data will be collected:

- Demographic and baseline characteristics (e.g. age, gender, pre-fracture mobility) Pre-injury quality of life (EQ5D) and at 30 and 120 days postoperatively
- Routine 'operation notes', perioperative complications, and discharge details
- The volume of blood that was autotransfused, when this was possible
- The number of donor blood units transfused and the date of transfusion will be collected
- Haemoglobin concentration
- Pre and postoperative delirium assessment
- Details of admission, assessment and treatment
- Contact details, including of carers when appropriate
- Complications and SAEs during the study period

Following their 120-day questionnaire, patients will have completed their participation in the trial and will continue to be treated as per normal standard of care.

#### Intervention Type

Procedure/Surgery

#### Primary outcome(s)

Current primary outcome measure as of 08/04/2020:

Health-related quality of life measured using the EuroQol 5 dimension(EQ-5D-5L) score at baseline (retrospective pre-fracture status) and 4 months post-operatively

Previous primary outcome measure:

- 1. Recruitment rate per centre
- 2. The number of patients for whom autotransfusion is possible
- 3. The volume of blood autotransfused

#### Key secondary outcome(s))

Current secondary outcome measures as of 08/04/2020:

- 1. Health-related quality of life measured using the EuroQol 5 dimension(EQ-5D-5L) score at baseline and 12 months post-operatively
- 2. Post-operative delirium risk measured using 4AT at baseline

- 3. Residential status measured using NHFD questions at 4 and 12 months post-surgery
- 4. Mobility measured using NHFD questions at 4 and 12 months post-surgery
- 5. Allogenic blood usage measured using hospital records at baseline
- 6. Mortality measured using death notifications from hospital records at 4 and 12 months postoperatively
- 7. Haemoglobin concentration at baseline
- 8. Complications, measured using medical records (check any complication classified as adverse events on the protocol will be collected from recruitment until the 12 -month time point)
- 9. Costs and comparative cost-effectiveness measured using hospital records and resource use questionnaire at 4 and 12 months post-operatively

#### Previous secondary outcome measures:

- 1. Health-related Quality of life will be collected using the EuroQol 5 dimension(EQ-5D-5L) score. This will be collected at baseline(retrospective pre-fracture status), 30 and 120 days post-operatively.
- 2. Units of allogenic blood transfused, this information will be collected at baseline.
- 3. Mortality
- 4. Haemoglobin concentration, this information will be collected at baseline
- 5. Complications, any complication classified as adverse events on the protocol will be collected from recruitment until the 4-month time point.
- 5. Resource use, costs and comparative cost-effectiveness

#### Completion date

31/03/2023

# Eligibility

#### Key inclusion criteria

Participants of 60 years of age and older who have sustained a fracture of the hip who, in the opinion of the operating surgeon, would benefit from surgery

# Participant type(s)

Patient

# Healthy volunteers allowed

No

### Age group

Senior

#### Sex

All

#### Key exclusion criteria

- 1. Patients younger than 60 years of age
- 2. Patients undergoing percutaneous hip screw fixation
- 3. Patients who have sustained a pathological fracture
- 4. Patients for whom the treating surgeon has already elected to use cell salvage (for example Jehovah Witness)

# Date of first enrolment

01/10/2019

#### Date of final enrolment

30/11/2021

# Locations

#### Countries of recruitment

**United Kingdom** 

England

Wales

# Study participating centre University Hospital Coventry

University Hospitals Coventry & Warwickshire NHS Trust Clifford Bridge Road Coventry United Kingdom CV2 2DX

# Study participating centre John Radcliffe Hospital

Headley Way Oxford United Kingdom OX3 9DU

#### Study participating centre Royal Berkshire NHS Foundation Trust

Royal Berkshire Hospital London Road Reading United Kingdom RG15AN

#### Study participating centre Medway Maritime Hospital Medway NHS Foundation Trust Windmill Road Gillingham

United Kingdom ME7 5NY

# Study participating centre St George's Hospital

Blackshaw Road London United Kingdom SW17 0QT

# Study participating centre Royal Derby Hospital

University Hospitals of Derby and Burton NHS Foundation Trust Uttoxeter Road Derby United Kingdom DE22 3NE

#### Study participating centre Queen's Medical Centre

Nottingham University Hospitals NHS Trust Derby Road Nottingham United Kingdom NG7 2UH

# Study participating centre Whipps Cross Hospital

Leytonstone London United Kingdom E11 1NR

# Study participating centre

North Tyneside General Hospital City Northumbria Healthcare NHS Foundation Trust North Shields United Kingdom

NE29 8NH

# Study participating centre Pinderfields Hospital

Aberford Road Wakefield United Kingdom WF1 4DG

# Study participating centre University Hospital of Wales

Heath Park Cardiff United Kingdom CF14 4XW

#### Study participating centre Southmead Hospital

Southmead Road Bristol United Kingdom BS10 5NB

#### Study participating centre Doncaster Royal Infirmary

Armthorpe Road Doncaster United Kingdom DN2 5LT

# Study participating centre Royal Derby Hospital

Uttoxeter Road Derby United Kingdom DE22 3NE

# Study participating centre University Hospital Of North Durham

North Road Durham County Durham United Kingdom DH1 5TW

Study participating centre
The Grange University Hospital

Caerleon Road Llanfrechfa Cwmbran United Kingdom NP44 8YN

# Sponsor information

#### Organisation

University Hospitals Coventry and Warwickshire NHS Trust

#### **ROR**

https://ror.org/025n38288

# Funder(s)

#### Funder type

Government

#### Funder Name

NIHR Central Commissioning Facility (CCF); Grant Codes: PB-PG-0817-20037

# **Results and Publications**

#### Individual participant data (IPD) sharing plan

Reasonable requests for access to the datasets can be made to Prof Xavier Griffin (X. griffin@qmul.ac.uk), three years after the publication of the clinical results of the study.

# IPD sharing plan summary

Available on request

#### Study outputs

Output typeDetailsDate createdDate addedPeer reviewed?Patient-facing?Protocol article08/06/202209/06/2022YesNoHRA research summary28/06/2023NoNo

Participant information sheetParticipant information sheet11/11/202511/11/2025NoYesStudy website11/11/202511/11/2025NoYes