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Study of the effectiveness and safety of treatments to help patients with anaemia recover from major emergency surgery. Perioperative Iron and ESA Intervention Study (POP-I)

Submission date
29/04/2023

Recruitment status
Recruiting

Registration date
20/10/2023

Overall study status
Ongoing

Last Edited
18/02/2026

Condition category
Haematological Disorders

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

Plain English summary of protocol

Background and study aims
Each year over 100,000 people over 60 years of age in the UK are admitted to hospital for lifesaving emergency operations. Two of the most common emergency operations are for hip fracture and severe abdominal problems. Many of these people have anaemia(a reduced number of red blood cells). Anaemia increases the risk of dying after surgery and those that do survive have a slower recovery, more complications, and therefore spend more time in hospital. Anaemia can be treated with drugs such as iron, but whether this improves survival and the general health of people who require an emergency operation is not known. Our aim is to improve outcomes for people who are anaemic following emergency surgery, and to determine the cost-effectiveness of drug treatment for anaemia compared with usual care.
One treatment option is a single infusion of iron, given through a drip. Another treatment option is to give iron plus an Erythropoiesis-Stimulating-Agent (ESA) called darbepoetin. An ESA works in combination with iron to increase the production of red blood cells and improve the blood count. This works in combination with iron to improve anaemia. Research in other groups of patients, such as those with heart and kidney problems, has shown that both treatments work very well. However, we do not know whether they would help patients recovering from emergency surgery.
We have designed a study to investigate whether treating anaemia after emergency surgery leads to people having more days at home after their operation.

Who can participate?
The study will recruit patients aged 60 years or older who have had different types of emergency surgery for abdominal problems or hip fracture.

What does the study involve?
The study will recruit patients who have had different types of emergency surgery for abdominal

problems or hip fracture. These patients will enter the study 1–10 days after their emergency operation and then assigned randomly(by chance) to one of three study groups: 1: usual care, 2: usual care + iron infusion 3: Usual care + iron infusion + ESA injection. We will also measure quality of life, safety, and cost or savings associated with either of the treatments.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Minor discomfort to a localised area if blood tests are taken, if subcutaneous injection of darbepoetin is given or if an intravenous infusion of iron is given.
Iron and ESAs are commonly used safe drugs, but the risks of infection with intravenous iron, and thrombosis with ESAs, remain unclear and both may be exacerbated if there is acute inflammation.
These risks will be minimised through monitoring of infection, thrombosis and other complications, reported as a secondary outcome at three time points. This data will be monitored throughout by the Data Monitoring Committee.

Where is the study run from?
Nottingham Clinical Trials Unit(UK)

When is the study starting and how long is it expected to run for?
April 2023 to April 2027

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

Who is the main contact?
Dr Iain Moppett, POP-I@nottingham.ac.uk

Contact information

Type(s)
Scientific

Contact name
None POP-I Team

Contact details
Applied Health Research Building
Building 42
Nottingham
United Kingdom
NG7 2RD
+44 115 8231600
POP-I@nottingham.ac.uk

Type(s)
Principal investigator

Contact name

Prof Iain Moppett

Contact details
Queen's Medical Center
Nottingham
United Kingdom
NG7 2RD
+44 115 823 0959
Iain.moppett@nottingham.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
1007432

Central Portfolio Management System (CPMS)
57530

Protocol serial number
23015

Study information

Scientific Title
The clinical benefits and cost effectiveness and safety of haematopoietic interventions for patients with anaemia following major emergency surgery: a Phase IV, multisite, multi-arm randomised controlled trial: Peri-op Iron and EPO Intervention Study (POP-I)

Acronym
POP-I

Study objectives
Primary objective:
To assess the clinical effectiveness of postoperative intravenous iron and intravenous iron plus injection of ESA (erythropoiesis stimulating agent) compared to a usual care control group respectively, for the treatment of anaemia across two major patient groups requiring emergency surgery.

Secondary objectives:
1. To monitor safety of the interventions.
2. To conduct an internal pilot to evaluate recruitment, uptake and retention rates, sample size parameter estimates, clinician protocol adherence, safety, adherence to treatment allocation, completeness, and quality of data collection.
3. To assess the cost effectiveness/cost utility of postoperative intravenous iron and intravenous iron plus ESA compared to a usual care control group respectively, and impact on resource use and quality of life from a healthcare, social care and broader societal viewpoint.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 16/10/2023, London - Hampstead Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8248; hampstead.rec@hra.nhs.uk), ref: 23/LO/0425

Study design
Interventional randomized parallel-group controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Postoperative anaemia

Interventions
The trial objective is to assess the clinical effectiveness of postoperative intravenous iron and intravenous iron plus a subcutaneous injection of an Erythropoiesis Stimulating Agent (ESA) compared to a usual care control group respectively, for the treatment of anaemia across two major patient groups who have had emergency surgery (i.e., hip fracture and emergency laparotomy).

The trial is a three-arm CTIMP that is predicated on two primary comparisons of (1) a monotherapy and (2) a combination therapy, compared with a single common control group (usual care) respectively, in a superiority hypothesis testing framework.
1. Usual Care (without additional anaemia therapy) is based upon care at sites aligned to national standards and guidelines including: NICE CG124, National Hip Fracture Database (NHFD), Association of Anaesthetists (hip fracture); National Emergency Laparotomy Audit (NELA) (emergency laparotomy); Best Practice Tariff (emergency laparotomy and hip fracture).
2. Iron Monotherapy consists of usual care (as above) plus intravenous Ferric Derisomaltose (approximately 20 mg/kg as a single dose before discharge).
3. Combination Iron and ESA consists of usual care plus intravenous Ferric Derisomaltose (as above) plus a subcutaneous injection of Darbepoetin (approximately 2 mcg/kg as a single dose before discharge).

Eligible participants will be randomised via a secure password-protected 24/7 website hosted by Nottingham Clinical Trials Unit. Allocation (ratio 1:1:1) will be assigned using a probabilistic minimisation algorithm balancing across the three groups on five important factors - recruiting site, type of surgery, age, sex, and postoperative haemoglobin concentration at randomisation.

Follow up takes place remotely at day 30 and day 120 post-randomisation. Follow up takes the from of a series of short questionnaires including:
1. Days at Home
2. Health related QoL (EQ-5D-5L)
3. Self-reported Mobility
4. Complications
5. Health Resource Usage

Intervention Type

Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Ferric derisomaltose, darbepoetin alfa

Primary outcome(s)
Days at home at 30 days (DAH30). Reported by participants or their personal legal representative or other person with close knowledge of the participant (e.g. staff from a nursing home), DAH30 is an integer between 0 and 30 that reflects, out of the 30 days following randomisation, the total number of those days that the participant spends alive and at home. DAH30 is derived by subtracting from 30 the duration of initial length of stay following randomisation, as well as the duration of any further readmissions (to hospital or elsewhere) in the first 30 days. All days spent not at home, other than holidays, are also subtracted. These include moving house to more dependent living, time spent with relatives, etc. If a participant never returns home or dies at any point within the first 30 days, they will be assigned a score of 0.

Key secondary outcome(s))
1. EQ-5D-5L. Reported by participants or their personal legal representative or other person with close knowledge of the participant (e.g. staff from a nursing home), the EuroQol-5 Dimension-5 Level (EQ-5D-5L) health status measure is a widely used generic instrument for describing and valuing health states. Measured at baseline, day 30, day 120.
2. NHFD Residential Status. Obtained from medical records at discharge. Categorised using the same ordinal scale as used by the NHFD: (1) own home/sheltered housing, (2) residential care, (3) nursing care, (4) rehabilitation unit – hospital bed in the current trust, (5) rehabilitation unit – hospital bed in another trust, (6) rehabilitation unit – NHS funded care home bed, and (7) acute hospital. Measured at discharge, day 30, day 120.
3. Walking Performance. Reported by participants or their personal legal representative or other person with close knowledge of the participant (e.g. staff from a nursing home), using the 'New Mobility Score', which has been utilised by the National Hip Fracture Database (NHFD). Measured at day 30, day 120.
4. Length of Stay. Length of stay is an integer that describes the number of days a patient was in hospital following randomisation. Calculated by obtaining the date of discharge from hospital records and then counting the number of nights between this date and the date of randomisation (obtained from study records). Measured at discharge, day 30, day 120.
5. Complications. Medical records for all patients will be reviewed by appropriately trained staff for indicators of infection at the time of the patient's discharge from the recruiting site. In addition, for those patients who have left hospital, the patients will self-report (via an online form, telephone interview or by post, at 30 and 120 days after randomisation) on any of the complications listed below. For those patients lacking capacity, their personal legal representative or other person with close knowledge of the participant (e.g. staff from a nursing home) will be asked to provide this information. Measured at discharge, day 30, day 120.
6. Hospital Resource/Cost Data. Obtained from hospital records, this measure defines the resources and cost associated with a patient's hospital episode. Measured at discharge.
7. Days alive and out of hospital at 30 days. Obtained from hospital records, 'Days alive and out of hospital' (DAOH30) is an integer between 0 and 30 which reflects, out of the 30 days following randomisation, the total number of those days that the participant spends alive and out of hospital. It is computed using Hospital Episode Statistics – Admitted Patient Care (HES-

APC) which captures date of discharge and readmissions within 30 days.
8. Health Resource Use Questionnaire – Post intervention costs healthcare/ social and societal. Reported by participants or their personal legal representative or other person with close knowledge of the participant (e.g. staff from a nursing home), this will be a purposely designed proforma to capture health and social care costs as well as costs from a societal and patient perspective (such as employment). Measured at baseline, day 30, day 120.
9. Mortality. Obtained from hospital records, or through linkage with NHS central records, mortality is a binary outcome that defines whether a patient has died between day 0 (randomisation) until day 120.

Completion date
30/04/2027

Eligibility

Key inclusion criteria
1. Age 60 years or older.
2. Hb 80–110 g/l measured on any day between day 1 and day 10 after surgery.
3. Major non-elective surgery in the last 1 to 10 days: Patient will have undergone either Emergency Laparotomy as defined by National Emergency Laparotomy Audit (NELA) OR Fragility Hip Fracture surgery as defined by National Hip Fracture Database (NHFD).

• Written informed consent from participant or personal legal representative.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
60 years

Upper age limit
100 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Use of intravenous iron, darbepoetin or other ESAs in last 30 days
2. Haematological diagnoses where iron overload is a risk (e.g., haemochromatosis or alpha-thalassaemia trait) or alternative treatments are indicated (e.g., haematological malignancies)
3. Acute uncontrolled infection as judged by the treating clinician (e.g. ongoing bacteraemia or

non-resolving sepsis) or patient expected to be on non-prophylactic antibiotics for greater than 14 days
4. Contraindication to thromboprophylaxis
5. Direct contraindications to IMP:
5.1. Disturbances of iron, iron overload
5.2. Uncontrolled hypertension
5.3. Red cell aplasia
5.4. Decompensated/severe chronic liver disease (Child Pugh C)
5.5. Advanced cancer (metastatic and/or receiving chemo/radiotherapy)
6. Patient not expected to survive for 30 days
7. Renal replacement therapy
8. Immunosuppressive therapy for organ transplant

Date of first enrolment
01/08/2023

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Queens Medical Centre, Nottingham University Hospital
Derby Road
Nottingham
England
NG7 2UH

Study participating centre
Nottingham City Hospital NHS Trust
Hucknall Road
Nottingham
England
NG5 1PB

Study participating centre
The Royal Victoria Infirmary
Queen Victoria Road

Newcastle upon Tyne
England
TS1 4LP

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

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
England
BN2 5BE

Sponsor information

Organisation
Nottingham Clinical Trials Unit

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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

Individual participant data (IPD) sharing plan

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?
Participant information sheet	version 1.0	27/06/2023	12/09/2024	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes