

# A multi-centre randomised controlled trial of the effects of a reduction in the threshold for blood transfusion following heart surgery

<b>Submission date</b> 01/09/2008	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 09/09/2008	<b>Overall study status</b> Completed	<input checked="" type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 22/02/2018	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Unnecessary blood transfusions increase healthcare costs both directly, because blood is an increasingly scarce and expensive resource, and indirectly, due to complications associated with transfusion. Transfusion may cause complications by reducing patients' ability to fight off infection and respond to the stress that surgery puts on the body, as well as (rarely) by transmitting viral infections present in donor blood. In the UK, cardiac (heart) surgery uses more than 6% of all donor blood. Although the benefits of red cells for managing life-threatening bleeding are clear, the majority of decisions to transfuse after surgery are made on the basis of a patient's haemoglobin (Hb) level - a measure of the ability of the blood to transport oxygen around the body. The level that causes a doctor to transfuse a patient varies widely, and studies in non-cardiac surgical fields have shown that lowering the level that 'triggers' transfusion (threshold) reduces complications as well as the use of blood. The aim of this study is to find out whether lowering the threshold for red cell transfusion reduces complications and NHS costs.

### Who can participate?

Patients aged over 16 undergoing cardiac surgery, whose Hb level drops below the level at which transfusion is conventionally given

### What does the study involve?

Participants are randomly allocated either to have decisions made about transfusion more or less as they are now, or to only have a transfusion when their Hb level drops to a lower 'restrictive' level. We assess the number of infectious complications (septicaemia, wound or chest infection) and ischaemic complications (stroke, heart attack or kidney failure) that occur during the first 3 months after surgery.

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

We believe that withholding transfusion until the lower Hb level is reached will reduce both complications and hospital costs. Participants will not need to have any special investigations or extra hospital visits.

Where is the study run from?  
Bristol Heart Institute (UK)

When is the study starting and how long is it expected to run for?  
December 2008 to November 2011

Who is funding the study?  
Health Technology Assessment Programme (UK)

Who is the main contact?  
Prof. Barney Reeves

## Contact information

**Type(s)**  
Scientific

**Contact name**  
Prof Barney Reeves

**Contact details**  
Bristol Heart Institute  
University of Bristol  
Level 7  
Queen's Building  
Upper Maudlin Street  
Bristol  
United Kingdom  
BS2 8HW

## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**  
HTA 06/402/94

## Study information

**Scientific Title**  
A multi-centre randomised controlled trial of Transfusion Indication Threshold Reduction on transfusion rates, morbidity and healthcare resource use following cardiac surgery

**Acronym**  
TITRe 2

## Study objectives

Current information as of 01/09/2009:

The hypothesis for the trial is that lowering the transfusion threshold for red cell transfusion from a haemoglobin (Hb)/haematocrit (Hct) level of 9 g/dL / 27 ('liberal', similar to current practice) to 7.5 g / dL / 22 ('restrictive') will reduce postoperative morbidity and NHS costs.

Information at time of registration:

The hypothesis for the trial is that lowering the transfusion threshold for red cell transfusion from a haemoglobin (Hb) level of 9 g/dL ('liberal', similar to current practice) to 7.5 g/dL ('restrictive') will reduce postoperative morbidity and NHS costs.

More details can be found at: <http://www.nets.nihr.ac.uk/projects/hta/0640294>

Protocol can be found at: [http://www.nets.nihr.ac.uk/\\_\\_data/assets/pdf\\_file/0003/51393/PRO-06-402-94.pdf](http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0003/51393/PRO-06-402-94.pdf)

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

1. First approved by Oxfordshire Regional Ethics Committee (REC) C on 31/10/2008 (ref: 08/H0606/125). Subsequent amendments were approved on 19/05/2009 and 14/07/2009.
2. The latest amendments included in this record were approved by the REC on 30/07/2010. Two further amendments were approved by the REC on 09/10/2009 and 12th April. These amendments do not affect the information shown on the ISRCTN page.

## Study design

Multicentre randomised controlled trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## 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

Patients undergoing cardiac surgery

## Interventions

Current information as of 01/09/2009:

The trial will compare two Hb thresholds for blood transfusion, 'liberal' and 'restrictive'. The thresholds are defined as follows:

A: Liberal (control, similar to current practice): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb / Hct level falls below 9.0 g / dL / 27. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb / Hct level above 9.0 g / dL / 27.

B: Restrictive (experimental): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb / Hct level falls below 7.5 g / dL / 22. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb / Hct level above 7.5 g / dL / 22.

Clinicians will be allowed to transfuse, or refuse to transfuse, in contravention of these thresholds but must document the reason(s).

The total duration of follow-up for each participant is 3 months post randomisation, at which point participants will leave the study. However, we are hoping to collect long-term mortality data from data held routinely by the NHS and will be seeking consent from participants for this.

Initial information at time of registration:

The trial will compare two Hb thresholds for blood transfusion, 'liberal' and 'restrictive'. The thresholds are defined as follows:

A: Liberal (control, similar to current practice): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb level falls below 9.0 g/dL. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb level above 9.0 g/dL.

B: Restrictive (experimental): participants randomised to this group will be eligible for transfusion if their post-operative nadir Hb level falls below 7.5 g/dL. One unit of RBC should be transfused and the Hb level checked before transfusing another unit. The objective should be to maintain the Hb level above 7.5 g/dL.

Clinicians will be allowed to transfuse, or refuse to transfuse, in contravention of these thresholds but must document the reason(s).

The total duration of follow-up for each participant is 3 months post randomisation, at which point participants will leave the study. However, we are hoping to collect long-term mortality data from data held routinely by the NHS and will be seeking consent from participants for this.

## **Intervention Type**

Procedure/Surgery

## **Phase**

Not Specified

## **Primary outcome measure**

Current information as of 01/09/2009:

A composite of serious infectious or ischaemic events in the first 3 months after randomisation. The infectious and ischaemic events to be recorded will include the following:

1. Infectious events:
  - 1.1. Sepsis
  - 1.2. Wound infection

- 2. Ischaemic events:
  - 2.1. Permanent stroke
  - 2.2. Myocardial infarction
  - 2.3. Acute kidney injury
  - 2.4. Gut infarction

Initial information at time of registration:

A composite of serious infectious or ischaemic events in the first 3 months after randomisation. The infectious and ischaemic events to be recorded will include the following:

- 1. Infectious events:
  - 1.1. Septicaemia
  - 1.2. Lower respiratory tract infection
  - 1.3. Urinary sepsis
  - 1.4. Wound infection
- 2. Ischaemic events:
  - 2.1. Permanent stroke
  - 2.2. Myocardial infarction
  - 2.3. Renal failure
  - 2.4. Gut infarction

### **Secondary outcome measures**

Current information as of 01/09/2009:

- 1. Units of red blood cells transfused, recorded for the duration of hospital stay post-randomisation
- 2. Proportion of patients experiencing an infectious event
- 3. Proportion of patients experiencing an ischaemic event
- 4. EuroQol EQ-5D
- 5. Duration of ICU/HDU stay post-operatively
- 6. Duration of post-operative hospital stay
- 7. All cause mortality, recorded for duration of participation in study (3 months post-randomisation)
- 8. Cumulative resource use, cost, and cost-effectiveness, assessed for duration of participation in study (3 months post-randomisation)

Initial information at time of registration:

- 1. Units of red blood cells transfused, recorded for the duration of hospital stay post-randomisation
- 2. Frequency of infectious events, recorded for the duration of hospital stay post-randomisation
- 3. Frequency of ischaemic events, recorded for the duration of hospital stay post-randomisation
- 4. EuroQol EQ-5D, assessed at baseline (pre-randomisation) and 3-months follow-up
- 5. Length of ICU stay, recorded for the duration of hospital stay post-randomisation
- 6. Length of hospital stay
- 7. All cause mortality, recorded for duration of participation in study (3 months post-randomisation)
- 8. Cumulative resource use, cost, and cost-effectiveness, assessed for duration of participation in study (3 months post-randomisation)

### **Overall study start date**

01/12/2008

**Completion date**

30/11/2011

## Eligibility

**Key inclusion criteria**

Current inclusion criteria as of 24/08/2010:

1. Adults of either sex, aged  $\geq 16$
2. Post-operative nadir Hb / Hct level below 9.0 g / dL / 27

Previous inclusion criteria from 01/09/2009 to 24/08/2010:

1. Adults of either sex, aged  $\geq 16$  and  $< 80$  years
2. Post-operative nadir Hb / Hct level below 9.0 g / dL / 27

Initial information at time of registration:

1. Adults of either sex, aged  $\geq 16$  and  $< 80$  years
2. Post-operative nadir Hb level below 9.0 g/dL

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

2,000

**Key exclusion criteria**

Current information as of 01/09/2009:

1. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g., Jehovah's Witnesses)
2. Patients with congenital or acquired platelet, red cell or clotting disorders
3. Patients with ongoing or recurrent sepsis
4. Patients who were unable to give full informed consent for the study (e.g., learning or language difficulties)
5. Patients with critical limb ischaemia
6. Patients undergoing emergency surgery
7. Patients already participating in another interventional research study

Initial information at time of registration:

1. Patients who are prevented from having blood and blood products according to a system of beliefs (e.g., Jehovah's Witnesses)
2. Patients with congenital or acquired platelet, red cell or clotting disorders
3. Patients with ongoing or recurrent systemic sepsis
4. Patients who were unable to give full informed consent for the study (e.g., learning or language difficulties)

5. Patients with a critical carotid artery stenosis (>75%) or critical limb ischaemia
6. Patients with flow limiting (>70% luminal stenosis) coronary artery disease not undergoing complete revascularisation

**Date of first enrolment**

01/12/2008

**Date of final enrolment**

30/11/2011

## Locations

**Countries of recruitment**

England

United Kingdom

**Study participating centre****Bristol Heart Institute**

Bristol

United Kingdom

BS2 8HW

## Sponsor information

**Organisation**

University Hospitals Bristol NHS Foundation Trust (UK)

**Sponsor details**

Research and Development Department

Education Centre

Level 3

Upper Maudlin Street

Bristol

England

United Kingdom

BS2 8AE

**Sponsor type**

Hospital/treatment centre

**Website**

<http://www.uhbristol.nhs.uk>

ROR

## Funder(s)

### Funder type

Government

### Funder Name

Health Technology Assessment Programme

### Alternative Name(s)

NIHR Health Technology Assessment Programme, HTA

### Funding Body Type

Government organisation

### Funding Body Subtype

National government

### Location

United Kingdom

## Results and Publications

### Publication and dissemination plan

Not provided at time of registration

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	01/06/2014		Yes	No
<a href="#">Statistical Analysis Plan</a>	statistical analysis plan	22/02/2015		No	No
<a href="#">Results article</a>	results	12/03/2015		Yes	No
<a href="#">Results article</a>	results	01/08/2016		Yes	No