RePHILL Trial

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RePHILL

A Multi-Centre Randomised Controlled Trial of Pre-Hospital Blood Product Administration versus Standard Care for Traumatic Haemorrhage

"Resuscitation with Pre-HospItaL BLood Products (PHBP)"

Protocol Version: 2.0, 16th January 2017

RePHILL

- **Sponsor:** University Hospitals Birmingham NHS Foundation Trust

- **Funding:** NIHR Efficacy & Mechanism Evaluation Programme (project number 14/152/14)

RePHILL

- Target number of patients nationally: **490**
- Length of recruitment: **3 ½ years**
- Length of follow-up: main trial data collection ends at **death, hospital discharge or at 30 days follow-up**, whichever occurs first
- Study funding duration: **4 years**

Jan 2018

- 4 Blood Banks – New X, UHCW, Addenbrooke's and Norfolk and Norwich
- 4 Air Ambulances – MAA, TAAS, MAGPAS and EAAA
- 8 Acute Trusts – UHB, UHCW, Addenbrooke's, Norfolk and Norwich, UHNM, Southmead, Notts QMC and Sheffield

Rationale

It is routine practice to give patients who have suffered major traumatic haemorrhage, blood products (blood and plasma) in hospital but there is insufficient good-quality evidence to support the use of blood products during resuscitation in a pre-hospital setting.

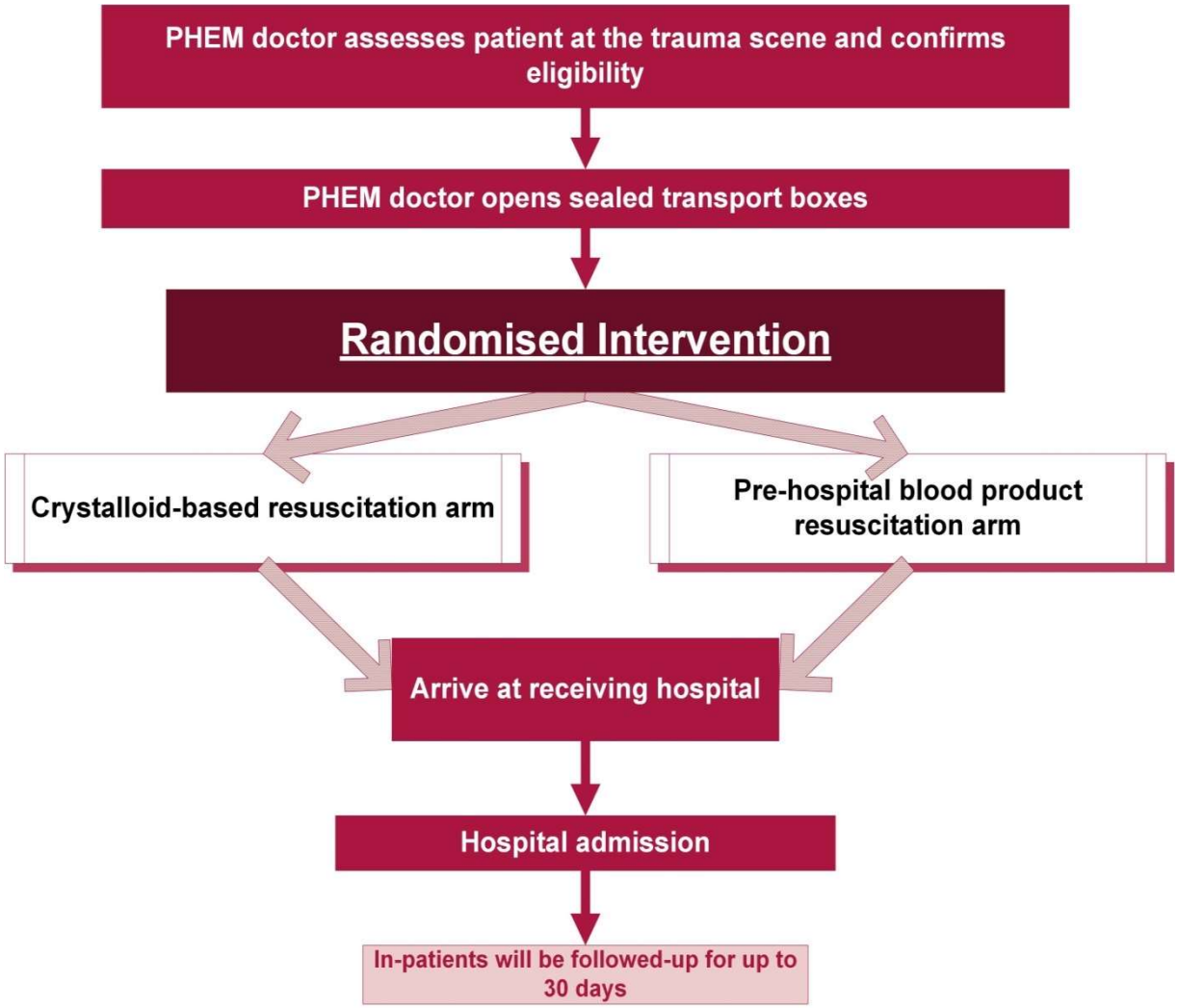
Primary objective

Investigate the clinical effectiveness of pre-hospital blood product (PHBP) resuscitation compared to the current standard care of restricted crystalloid-based resuscitation (standard care) in patients suffering from major traumatic haemorrhage.

Secondary objectives

- When compared to standard care, does PHBP resuscitation:
  - Improve blood pressure, heart rate and capillary oxygenation on ED arrival?
  - Prolong on-scene time?
  - Reduce pre-hospital fluid requirements?
  - Reduce in-hospital transfusion requirements?
  - Reduce trauma-induced coagulopathy?
  - Preserve platelet function?
  - Lead to a greater incidence of transfusion-related complications?
  - Lead to blood product wastage?

Summary


PHEM doctor assesses patient at the trauma scene and confirms eligibility
PHEM doctor opens sealed transport boxes
Randomised Intervention
Crystalloid-based resuscitation arm
Pre-hospital blood product resuscitation arm
Arrive at receiving hospital
Hospital admission
In-patients will be followed-up for up to 30 days

Inclusion criteria

- Traumatic injury
- Pre-Hospital Emergency Medical (PHEM) team attend
- Hypotension (defined criteria)

Exclusion criteria

- Children (known or apparently <16 y.o.)
- Blood administered on-scene prior to randomisation
- Refusal of blood product administration (e.g. known Jehovah's Witness)
- Pregnancy (known or apparent)
- Isolated head injury without evidence of external haemorrhage
- Known prisoners in the custody of HM Prison or Probation services

How?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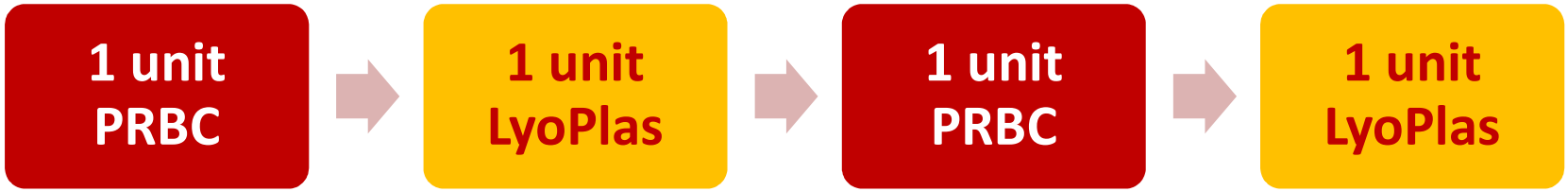
Standard care arm

Up to 4 boluses of 250mL sodium chloride 0.9% (normal saline), given sequentially.

PHBP arm

Up to 2 units of packed red blood cells (PRBC) and up to 2 units of lyophilised plasma (LyoPlas) given in the following order:



LyoPlas

- Manufactured by the German Red Cross (DRK)
- Freeze-dried plasma derived from a single donation
- Used in the same indication as FFP
- Can be stored between **+2 and +25 ˚C**
- Shelf life of **15 months**
- Classed as a **prescription-only medication** in Germany

Pharmacies receive LyoPlas and supply to the blood banks and maintain oversight throughout the trial

Blood banks store and pack LyoPlas, PRBC or saline into transport boxes and supply to PHEM teams

PHEM teams attend patient on-scene, deliver intervention and transfer patient to the receiving hospital

Receiving hospitals provide further treatment, obtain consent and complete follow-up for the patient

Primary outcome

The primary outcome is a composite measure consisting of:

1) Episode mortality
2) Lactate clearance. A failure to achieve lactate clearance on ≥ 20% per hour in the first 2 hours after randomisation

Secondary outcomes

- Individual components of the primary outcome
- All cause mortality within 3 hours of randomisation
- Pre-hospital fluid type and volume
- Vital signs at scene, on arrival at ED, then also at 2, 6 & 24 hours
- Trauma-induced coagulopathy
- Coagulation measured viscoelasticity by rotational thromboelastometry (ROTEM)
- Platelet function using electrode impedance aggregometry (Multiplate)

Key consideration

- **Patient consent**
  - Major traumatic haemorrhage is a life-threatening condition that requires urgent treatment
  - Majority of patients will lack capacity throughout recruitment and intervention periods
  - Clinically unjustifiable to delay treatment until fully informed consent can be obtained

Consequently, RePHILL cannot be conducted on the basis of prospective informed consent

Monitoring and audit

Trial Steering Committee

Independent supervision of the trial, including recruitment rates, compliance with trial drug, withdrawal, follow-up etc.

Data Monitoring Committee

Is the trial safe? Has a clear result been reached?

Inspections from MHRA and/or audits from Trust R&D Department

Definitions – serious

Any adverse event or adverse reaction that:

- Is life-threatening
- Results in death
- Requires hospitalisation or prolongs existing hospitalisation
- Results in persistent or significant disability or incapacity
- Consists of a congenital anomaly or birth defect

Definitions – unexpected

An adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product set out in the SmPC or IB for that product.

For the RePHILL trial, SmPCs will be provided for both LyoPlas and normal saline and will be used to assess expectedness.

Some stats

Gender split

	Number	%
Male	37	67.3%
Female	9	16.4%
Missing	9	16.4%
Total	55	100%

Some stats

Age

	Years (N=33)
Mean	34.6
Median	29
Range	18 to 78

Some stats

Mechanism of Injury