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NHS Blood and Transplant

What data are needed for blood collectors to provide cold-stored whole blood?

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Caring Expert Quality

Conflicts of interest

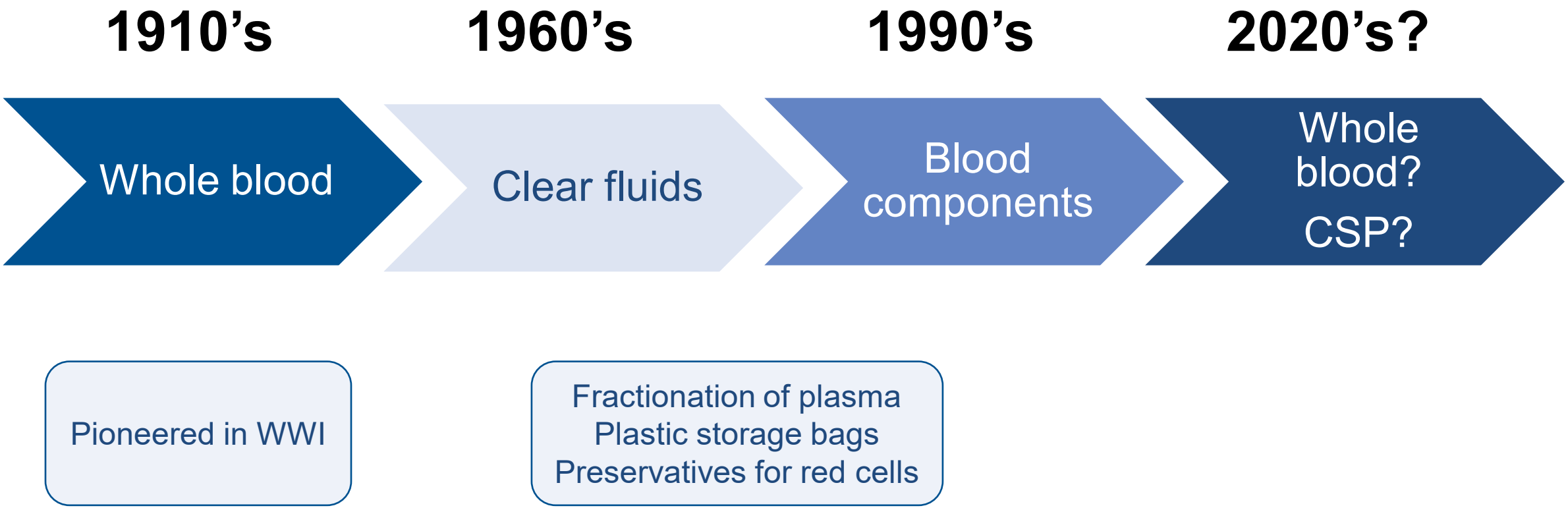
- I am a member of Terumo BCT's Advisory Board, who make filters for LD whole blood
- I work for a national blood provider!

Content

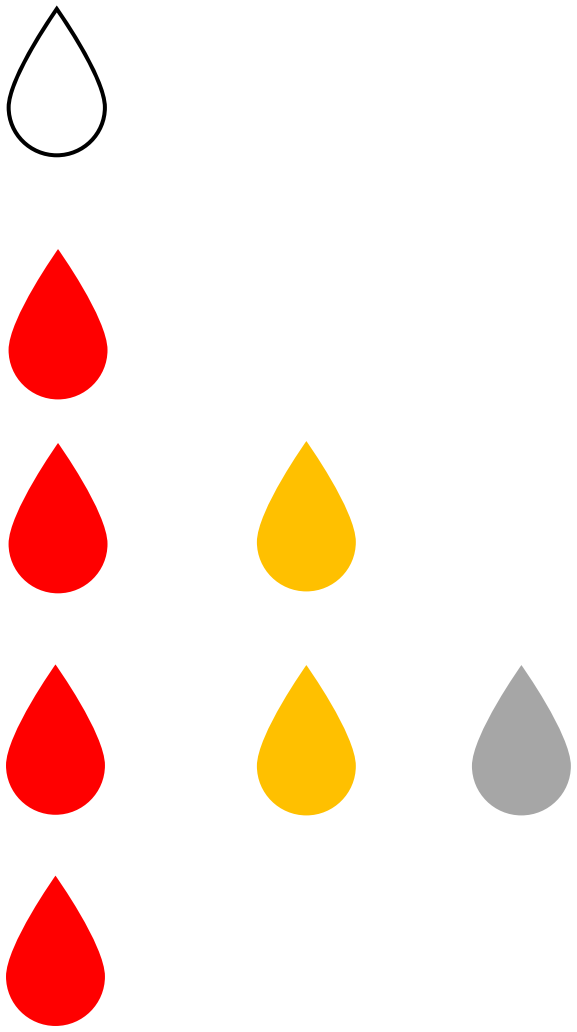
- What is the clinical need/benefit v current standard of care?
- Donor selection
- Manufacture and storage of the product
- Cost and logistics
- What are the outstanding research questions?

These considerations differ depending on current standard of care, nature of blood supplier & local societal considerations in relation to risk

Pre-hospital treatment of major haemorrhage has evolved



Pre-hospital protocols for resuscitation vary



clear fluids only

RBC

RBC + thawed/dried plasma

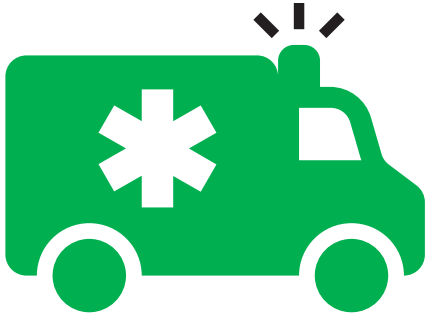
RBC + thawed/dried plasma + cold stored platelets

Whole blood

Perceived benefits of whole blood transfusion

Balanced resuscitation
1:1:1

Improved efficacy/reduced transfusion requirements



Simpler/reduced time to administer

Can we reduce the mortality of patients from traumatic major haemorrhage?

Evidence that WB is superior to component therapy is lacking

Emerg Med J. 2020 Jun;37(6):370-378. doi: 10.1136/emermed-2019-209040. Epub 2020 May 6.

Whole blood transfusion versus component therapy in adult trauma patients with acute major haemorrhage

Pascale Avery [1 2], Sarah Morton [3], Harriet Tucker [2 4 5], Laura Green [2 6 7], Anne Weaver [2 8 9], Ross Davenport [2 10]

Contents lists available at ScienceDirect

Blood Reviews

journal homepage: www.elsevier.com/locate/issn/0268960X

Review

Assessing the risks of haemolysis as an adverse reaction following the transfusion of ABO incompatible plasma-containing components - A scoping review

Josephine McCullagh [a,b,1,*], Rebecca Cardigan [c,g,1], Susan J. Brunskill [f], Tom Bullock [d], Carolyn Doree [f], Lise Estcourt [f], Sian Huish [c], Josie Sandercock [f], Laura Green [a,c,e]

[a] Barts Health NHS Trust, London, United Kingdom
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[d] Red Cell Immunohaematology NHS Blood and Transplant, United Kingdom
[e] Blizard Institute, Queen Mary University of London, London, United Kingdom
[f] Systematic Review Initiative, NHS Blood and Transplant, Oxford, United Kingdom
[g] Department of Haematology, University of Cambridge, United Kingdom

SYSTEMATIC REVIEW

Outcome measures used in clinical research evaluating prehospital blood component transfusion in traumatically injured bleeding patients: A systematic review

Tucker, Harriet FRCEM FIMC RCSEd; Avery, Pascale BMBS, Msc; Brohi, Karim FRCS, FRCA; Davenport, Ross FRCS, PhD; Griggs, Joanne MSc; Weaver, Anne FCEM; Green, Laura MD (Res), FRCP, FRCPath

Author Information

Journal of Trauma and Acute Care Surgery: December 2021 - Volume 91 - Issue 6 - p 1018-1024
doi: 10.1097/TA.0000000000003360

Transfusion Medicine Reviews
Volume 36, Issue 1, January 2022, Pages 7-15

Original Articles

The Difference in Potential Harms between Whole Blood and Component Blood Transfusion in major Bleeding: A Rapid Systematic Review and Meta-Analysis of RCTs

Louise J Geneen [a, b], Susan J Brunskill [a, b], Carolyn Doree [a, b], Lise J Estcourt [a, b, c], Laura Green [c, d, e]

Donor selection considerations

We need to mitigate the risk of group O plasma to non-O patients:

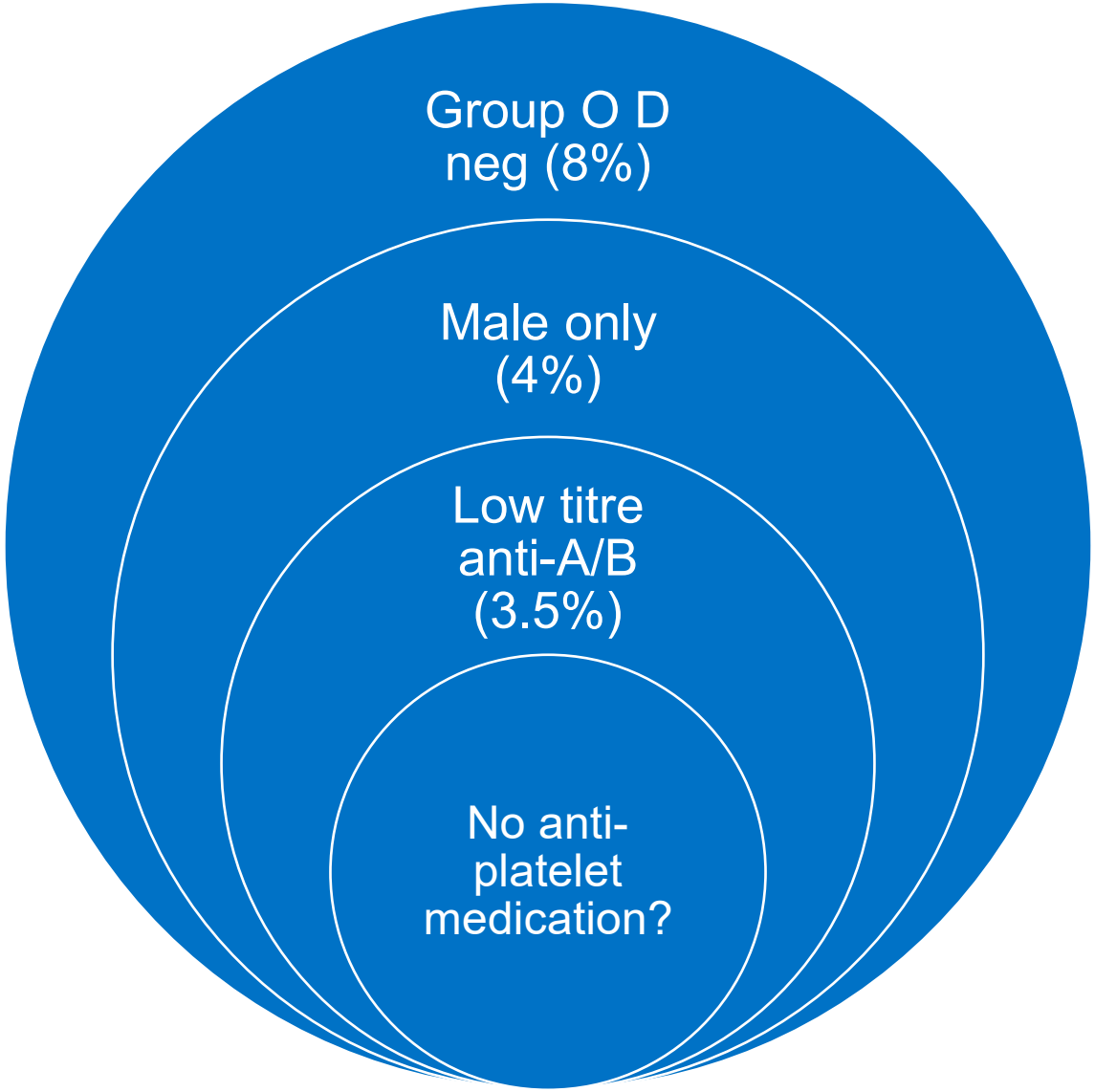
- TRALI – male only donors or females tested for HLA/HNA antibodies
- HTR – select donations that test as low titre for anti-A +B – not everyone is set up to do this routinely

- Choice of anticoagulants (CPDA-1 v CPD)

– D negative or positive, or both?

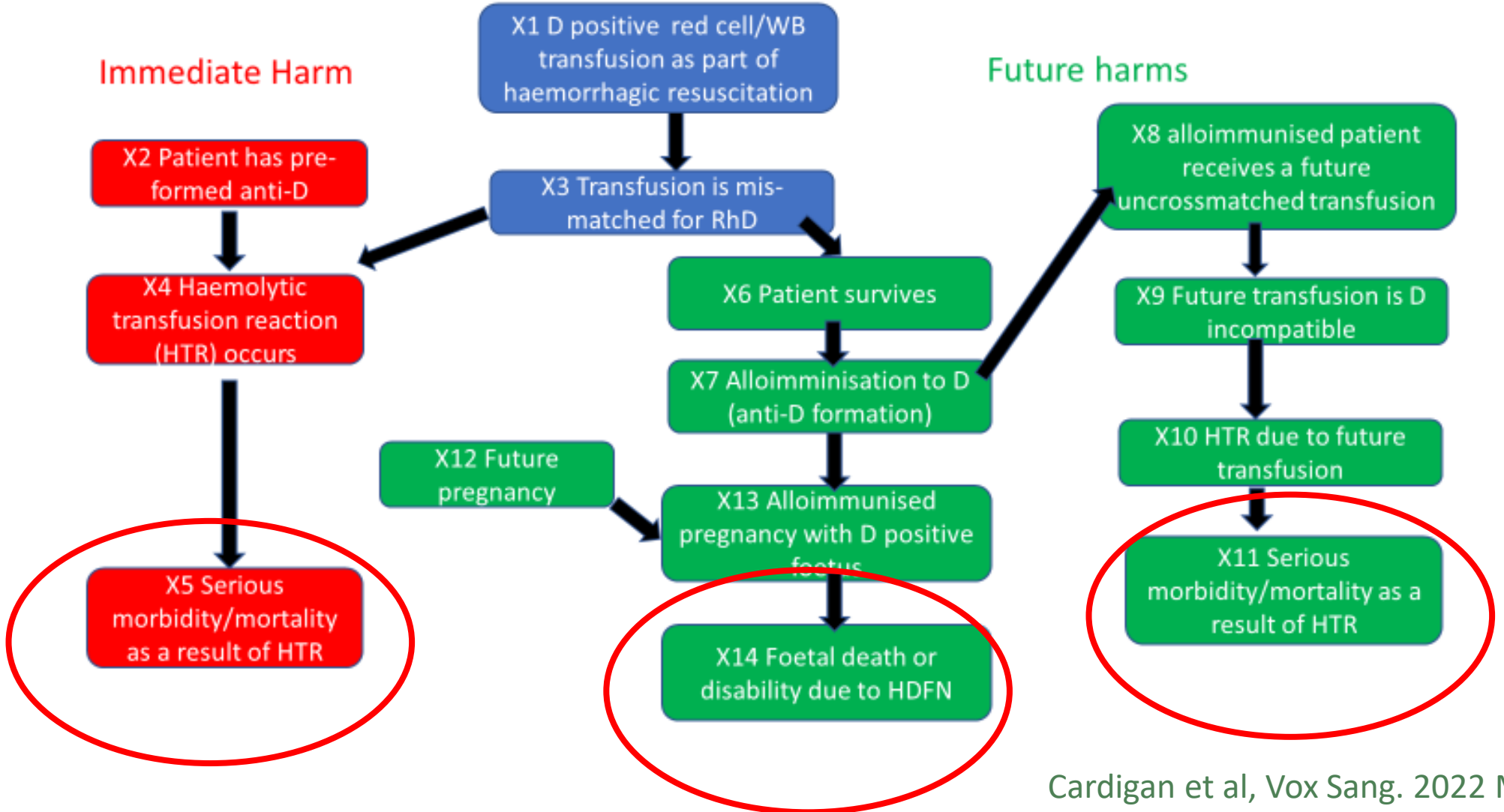
- For ‘non-standard’ LD filters collect in these bags or others?

Donor pool for WB is smaller than for red cells



What are the risks of using D positive blood?

Figure 1. Sequence of events required to cause harm from transfusion of RhD positive red cells in pre-hospital setting



Cardigan et al, Vox Sang. 2022 May;117(5):701-707

Modelling a change in policy from D n to D pos for England

Harm	All recipients 1 event every x tran (95% CI)	child sions
Major morbidity or mortality due to HTR from index D-positive transfusion	2.7x10[illegible]	[illegible]^3– 9.2x10^4)
Major morbidity or due to future	[illegible]	1.4x10^5 (3.1x10^4 – 3.7 x10^6)
Foetal d disabilit HDFN in f	[illegible]^4 – 1.2x10^5)	570 (260-2,300) 1:5 years
Any of above	1.4x10^4 (5.6x10^3 -4.2x10^4)	520 (250-1,700)

<1% improvement in mortality with WB would 'offset' life years lost due to HDFN risk

Cardigan et al, Vox Sang. 2022 May;117(5):701-707

Manufacturing considerations

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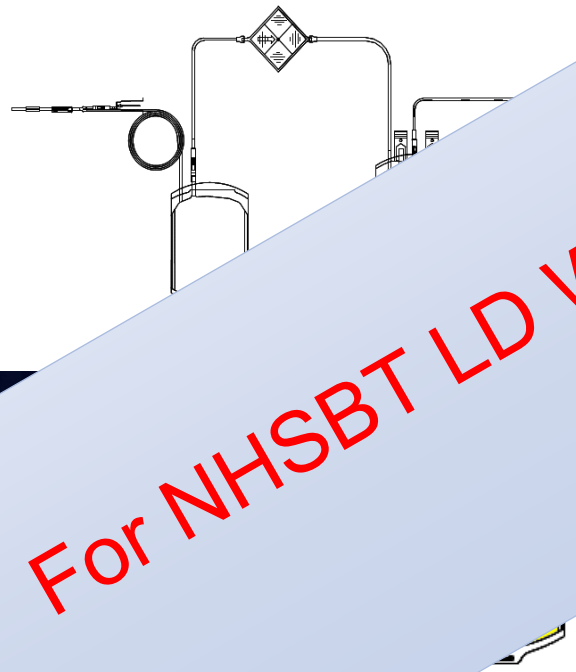
- Time from donation to processing – current IFU for Terumo does not cover 24H ambient hold
- To LD or not to LD, use of different collection packs & filters
- Shelf-life
- The move away from DEHP in the EU

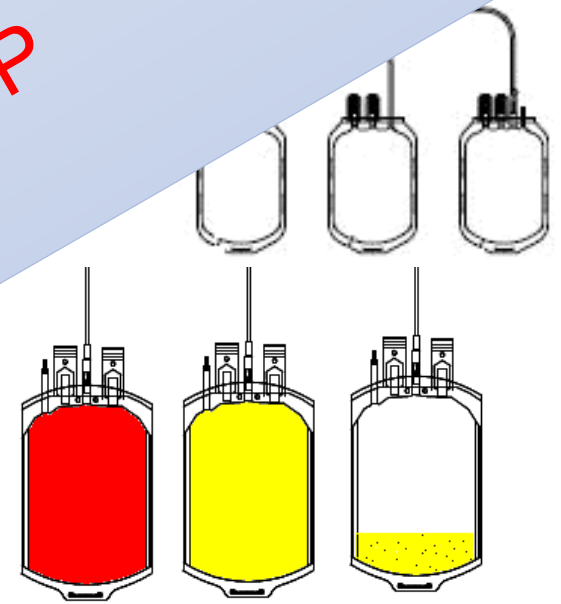
Special filters are needed to produ D WB containing platelet

Current

Leucodepletion filter removes platelets



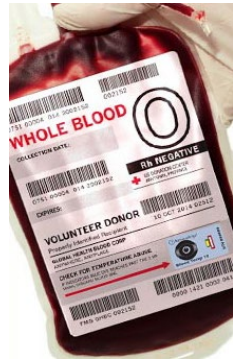
Plasma



Red cells

Plasma

¼ unit of platelets



For NHSBT LD WB likely 30% more expensive than RBC +FFP

Filters approx. 10 x more expensive

Shelf-life is shorter than standard red cells

RBC 35-42d

CPD WB 7-21d

Increased wastage

Options

- Recycle
- Use for non-trauma
- Use D pos

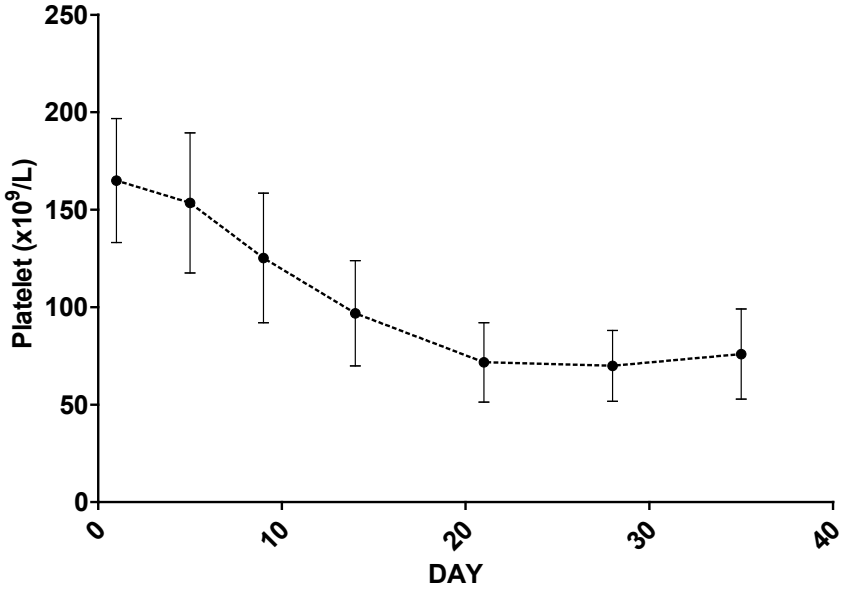
Shelf life of WB was determined by RBC viability

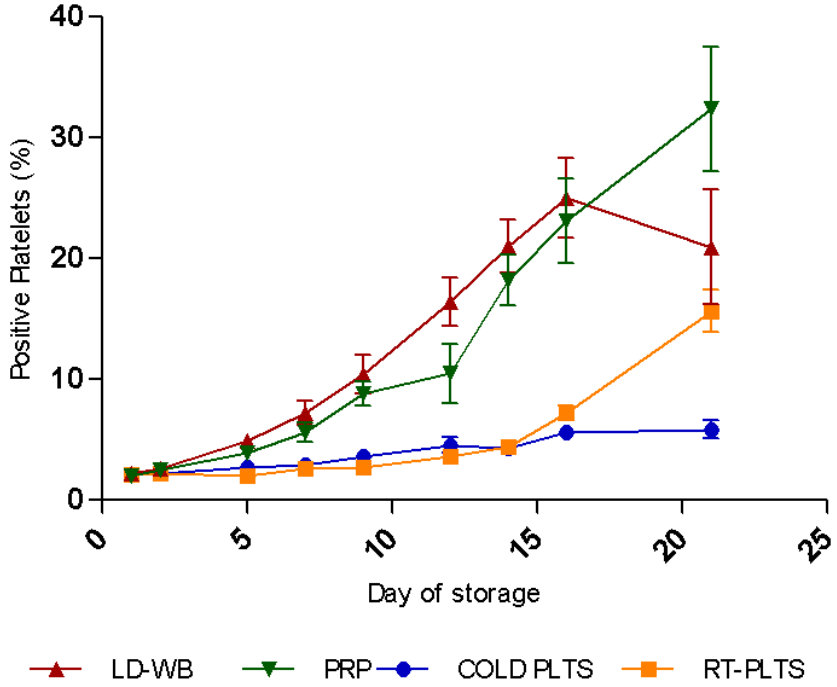
Historically based on FDA criteria of >75% of RBC remaining in circulation 24 following infusion to healthy volunteers

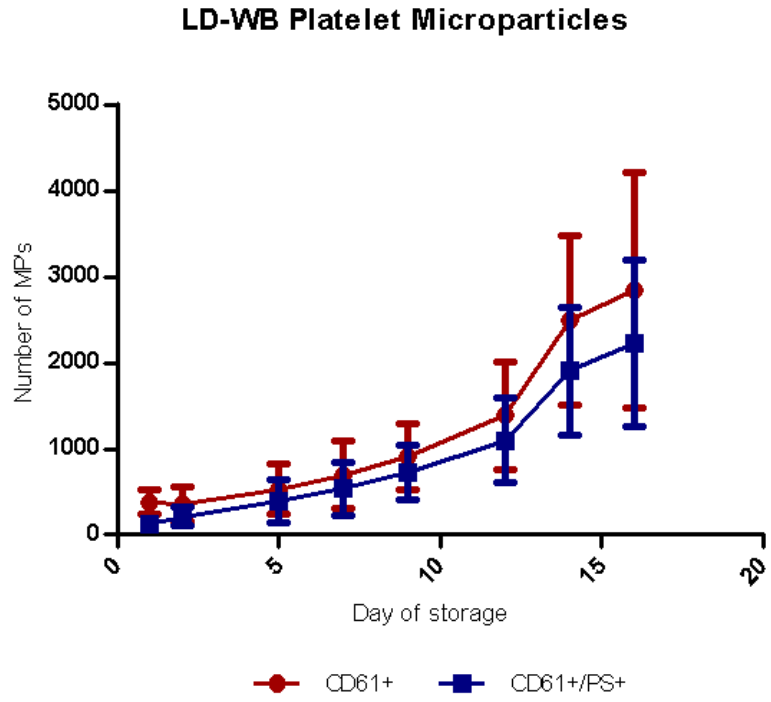
CPD WB	CPDA-1 WB	RBC in AS
21 days	35 days	35-42 days

Addtiion of adenine and more dextrose increases shelf life either in anticoagulant or AS

It’s difficult to know what its shelf life should be







Research Questions

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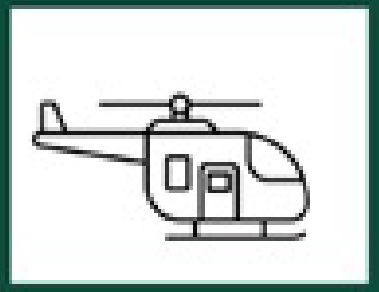
- Is WB superior to component therapy in the resuscitation of bleeding patients?
  - Relevant clinical outcomes – mortality, transfusion requirements
  - Logistical benefits, time on scene
- What is it's optimal shelf-life?
- Are the risks associated with use of D positive blood acceptable if D negative blood is unavailable?
  - What do patients and the public think?
- Is it cost-effective?

PPOWER pilot RCT USA n=86

PREHOSPTIAL LOW TITER GROUP O WHOLE BLOOD IS FEASIBLE AND SAFE: RESULTS OF A PROSPECTIVE RANDOMIZED PILOT TRIAL



Injured Patients in Hemorrhagic Shock

WB vs. Standard Care

Cluster Randomized

Exception From Informed Consent

Feasibility

Halted Enrollment
76% Target

Lower Than Expected Protocol Adherence
86%

Safety/Efficacy

25% vs 26.1%
28-day Mortality, p=0.8

Lower RBC needs
Lower TEG Abnormalities

Guyette et al. J Trauma Acute Care Surg 2022 May 1;92(5):839-847.

TOWAR Study USA

	Prospective RCT
Design	Randomised parallel assignment
Study population	Pre-hospital haemorrhagic shock
Participants	1020
Comparators	Up to 2 units WB pre-hospital versus standard of care
Primary endpoint	30d mortality
Secondary endpoints	Numerous including age of blood (1-14d v >14d)

Recruiting : Due to complete mid 2025

Source:clinicaltrials.gov

TSTORHM study - France

Design	Prospective RCT non-inferiority
Study population	Trauma triggering MTP
Sample size	164 (82 per arm)
Comparators	WB (up to 6 units) v component therapy
WB used	Terumo filter, 21d shelf-life, 'recycled at 7-14d'
Primary endpoint	MA by TEG
Secondary endpoints	Laboratory markers of haemolysis 2h & 30d mortality Units transfused

SWiFT study - England

Design	Prospective multi-centre unblinded RCT
Study population	Pre-hospital major traumatic haemorrhage
Sample size	848
Comparators	Wb (up to 2 units) v standard of care (RBC + plasma)
WB used	Terumo filter, 21d shelf-life
Primary endpoint	all-cause mortality or received ≥10 units of any blood components ≤24 hours from randomisation
Secondary endpoints	Morbidity & Mortality 30, 90 days Hospital resource to discharge Cost-effectiveness Health-related quality of life at 90 days Safety

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Thank you!

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