CRYOSTAT-2

EARLY CRYOPRECIPITATE IN TRAUMA

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on behalf of the CRYOSTAT-2 team

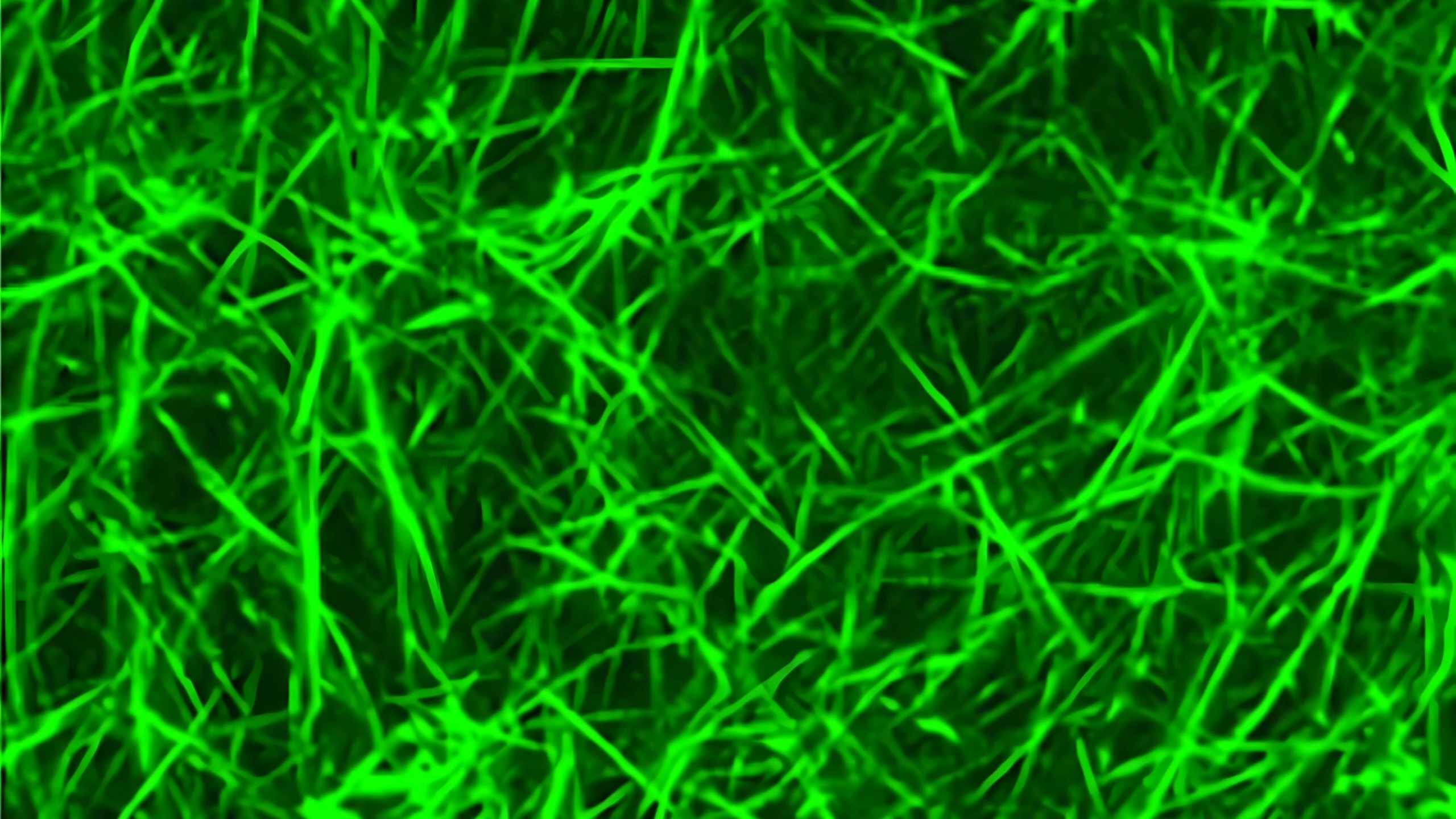
Queen Mary University of London

CENTRE FOR TRAUMA SCIENCES

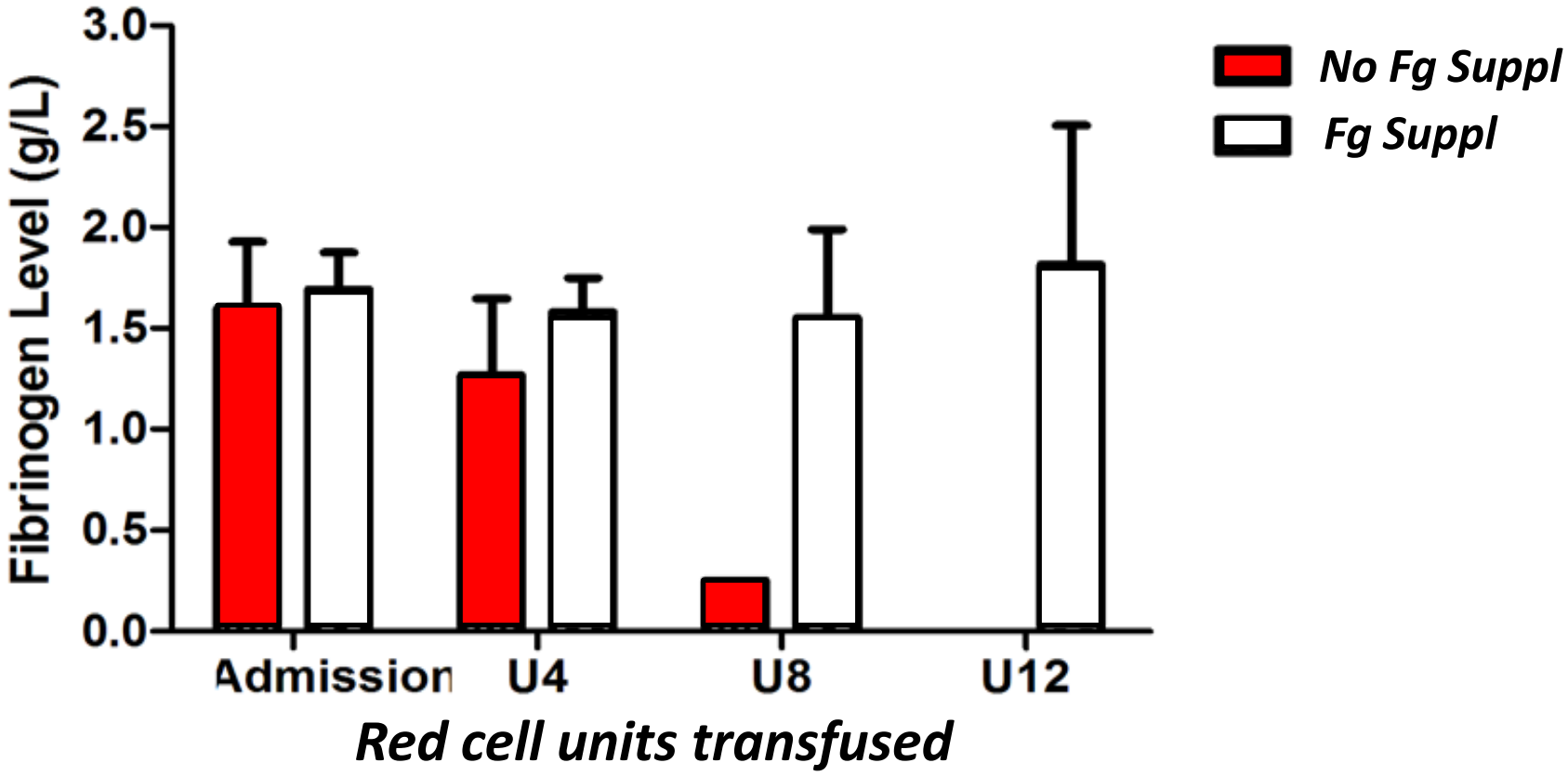
NHS Blood and Transplant

NHS National Institute for Health Research

barts CHARITY

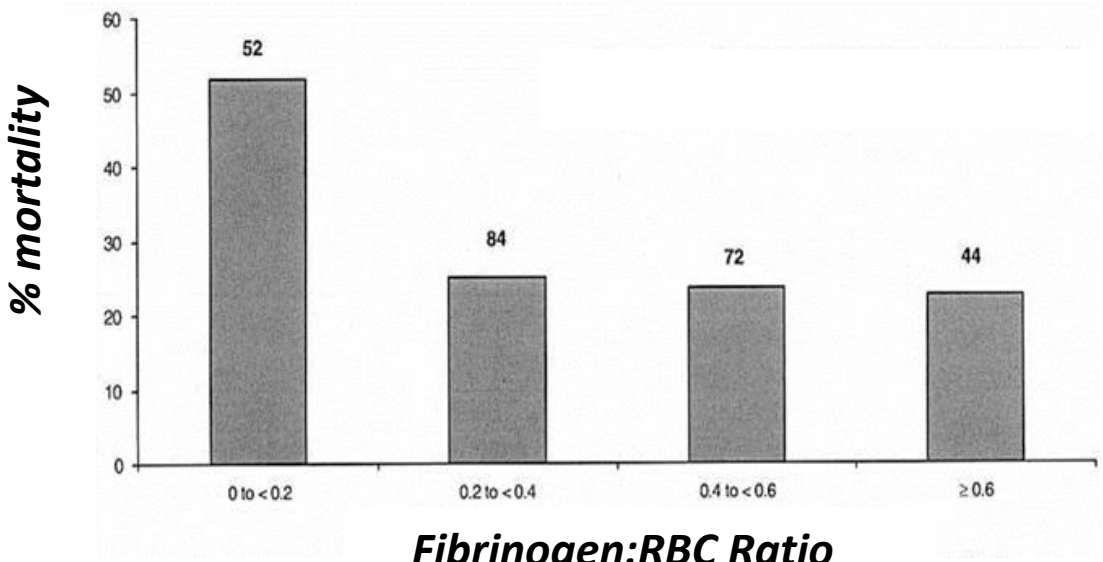


Fibrinogen levels in trauma patients during haemorrhage:

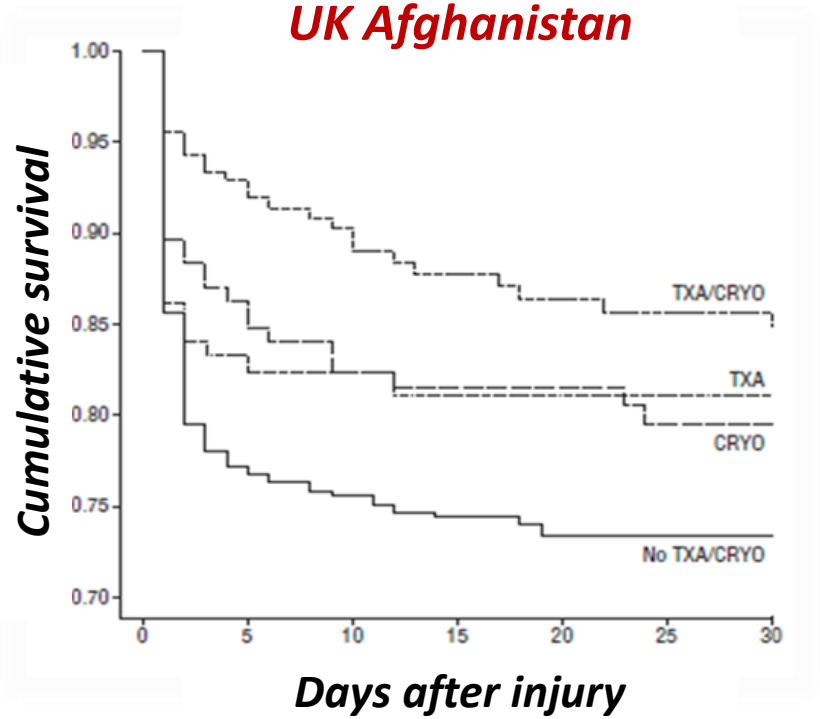


US & UK Military Cohort Studies:

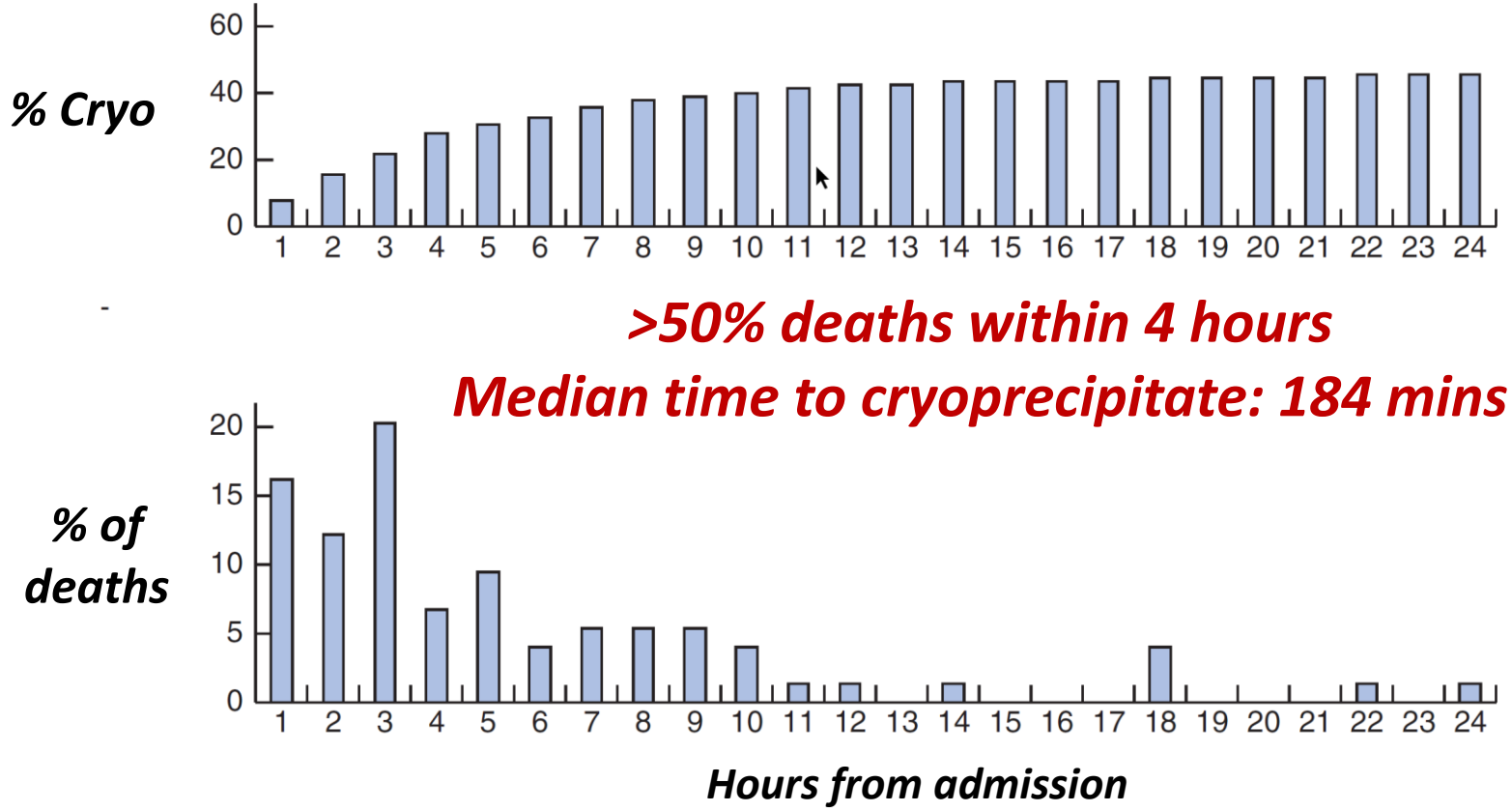
US Iraq



UK Afghanistan



UK National Trauma Transfusion Study:



>50% deaths within 4 hours

Median time to cryoprecipitate: 184 mins

CRYOSTAT-1

EARLY CRYOPRECIPITATE IN TRAUMA

Intervention group:

2 pools cryo <90 minutes of admission

Comparator group:

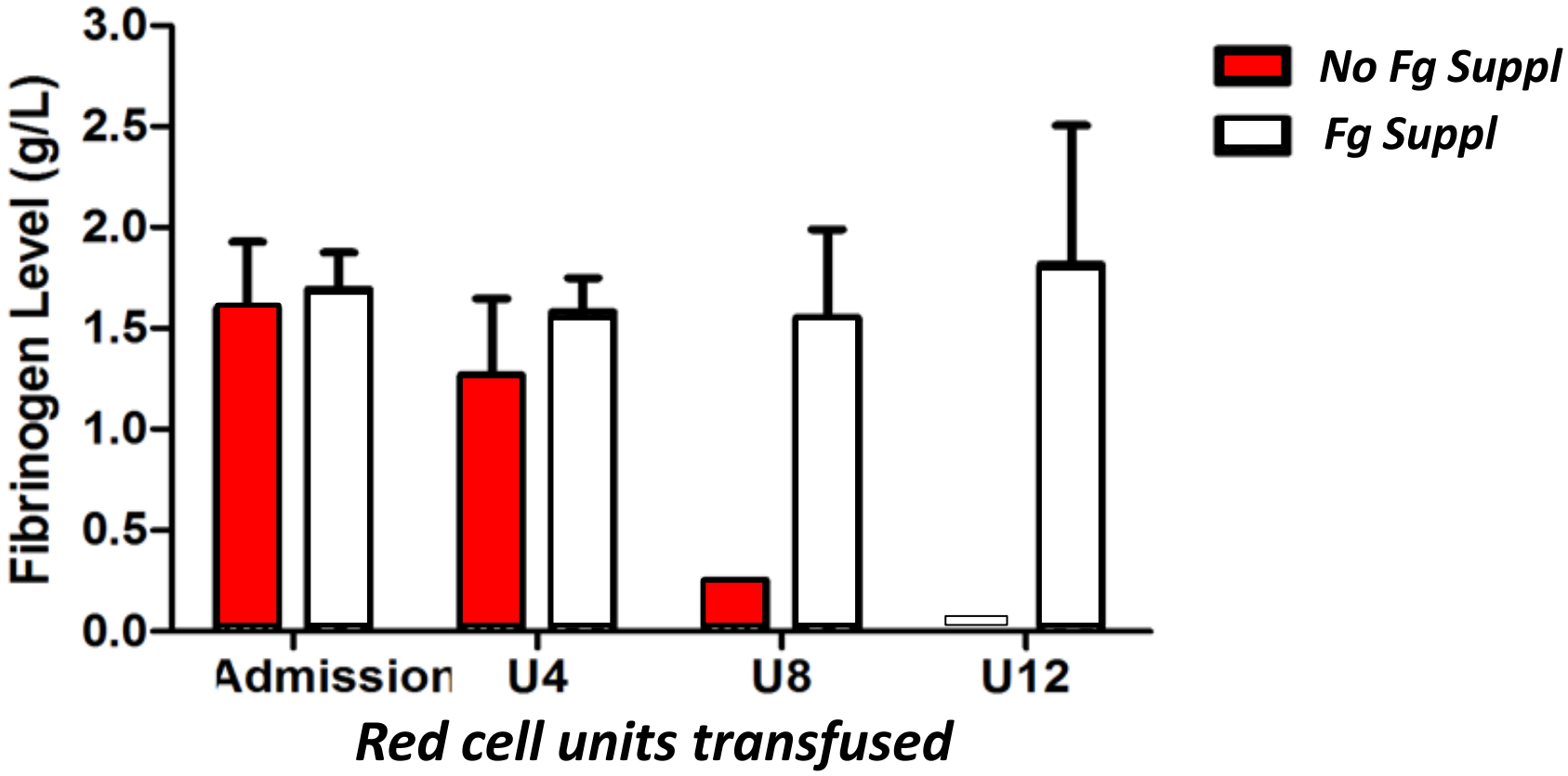
Standard major haemorrhage protocol

CRYOSTAT-1

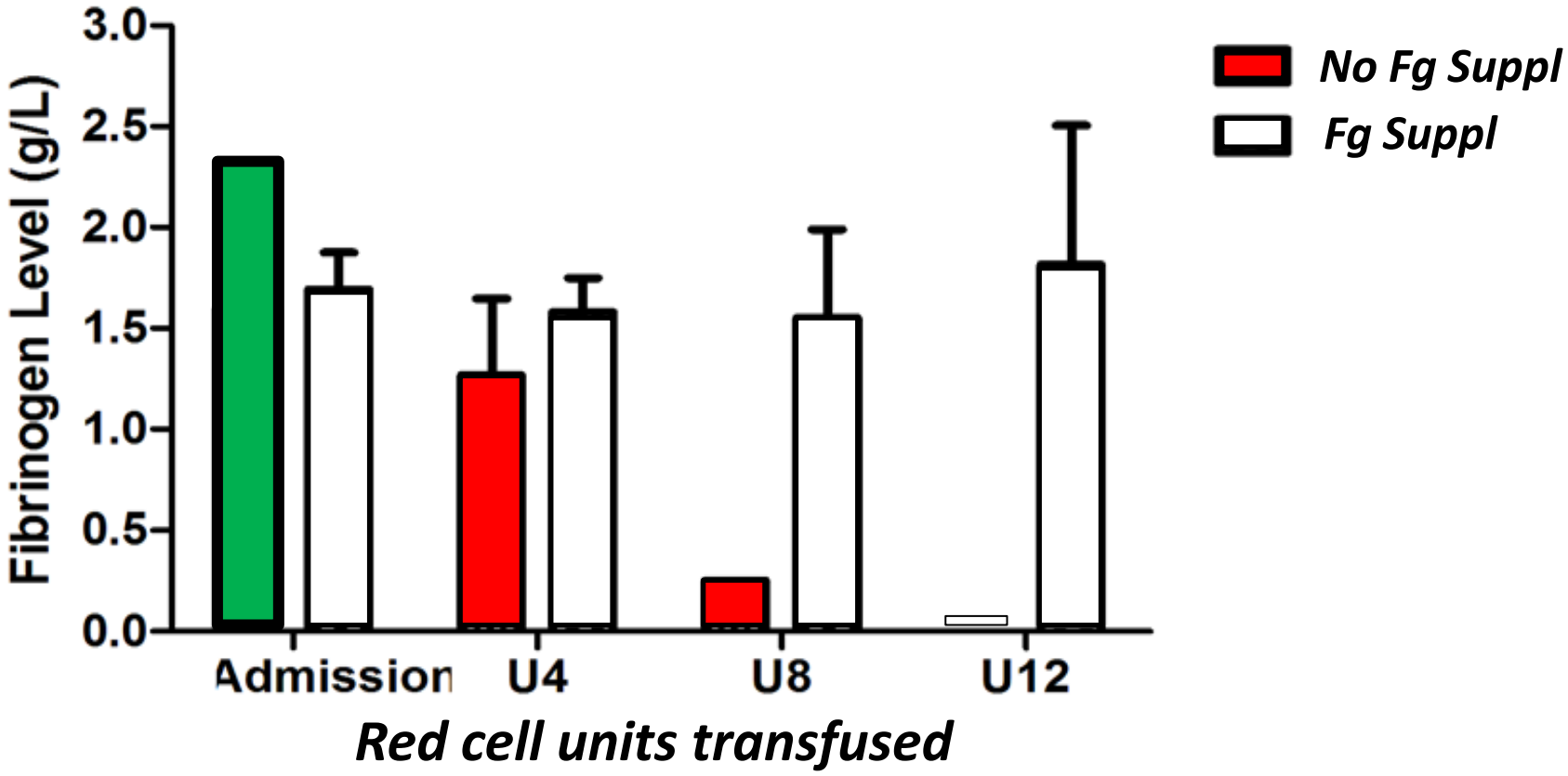
EARLY CRYOPRECIPITATE IN TRAUMA

	Std MHP (n=20)	Early Cryo (n=21)
Received cryo <90 minutes	29%	81%
Admission fibrinogen (g/dl)	1.55	1.60
Lowest fibrinogen (g/dl)	0.60	1.81
Mortality	28.6%	10.0%

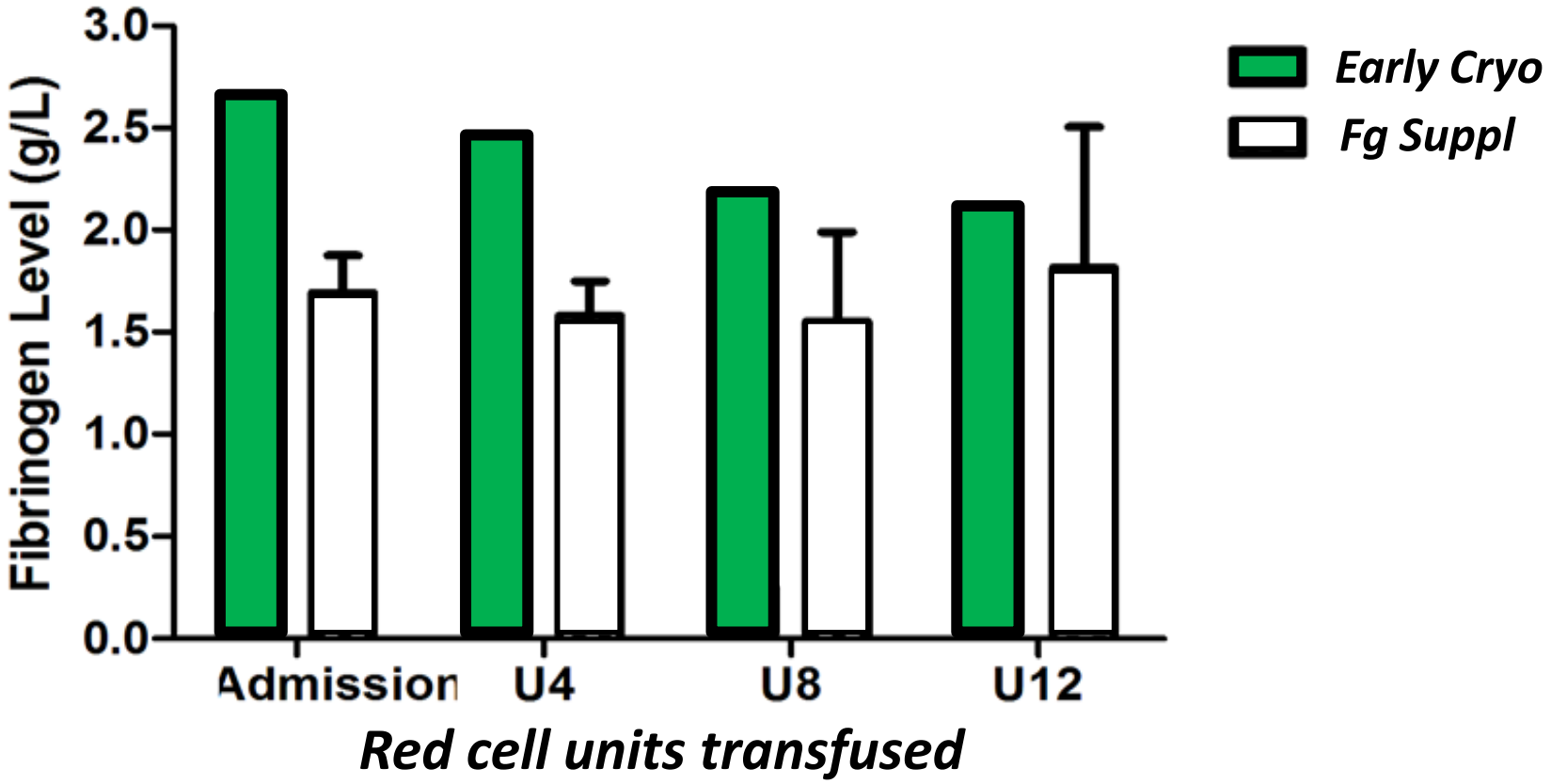
CRYOSTAT-2 TRIAL ETHOS:



CRYOSTAT-2 TRIAL ETHOS:



CRYOSTAT-2 TRIAL ETHOS:



CRYOSTAT-2

EARLY CRYOPRECIPITATE IN TRAUMA

A randomised controlled trial
in adult patients with major trauma haemorrhage
to evaluate the effects of early, empiric, administration of
3 pools of cryoprecipitate on mortality

CRYOSTAT-2 METHODS:

Inclusion criteria:

Adult patients affected by traumatic injury with
Suspected on-going active haemorrhage

AND has activated the local major haemorrhage protocol

AND has started or received at least one unit of any blood component

Exclusion criteria:

Transferred from another hospital or
Trauma team leader deems injury incompatible with life or
>3 hours from the time of injury

CRYOSTAT-2 METHODS:

Intervention:

3 pools of Cryoprecipitate (6g fibrinogen equivalent)
…as soon as possible
…in addition to standard local major haemorrhage protocol

Control:

Standard local major haemorrhage protocol

CRYOSTAT-2 METHODS:

Primary Outcome: *28-day all-cause mortality*

Secondary Outcomes:

- *All-cause mortality at 6 & 24 hours*
- *Death from bleeding at 6 & 24 hours*
- *Transfusion requirements @ 24 hours*

- *Mortality at 6 & 12 months*
- *EQ-5D-5L & GOSE at discharge and 6 months*
- *Hospital resource use up to discharge or day 28*

CRYOSTAT-2 METHODS:

Randomised, parallel-group

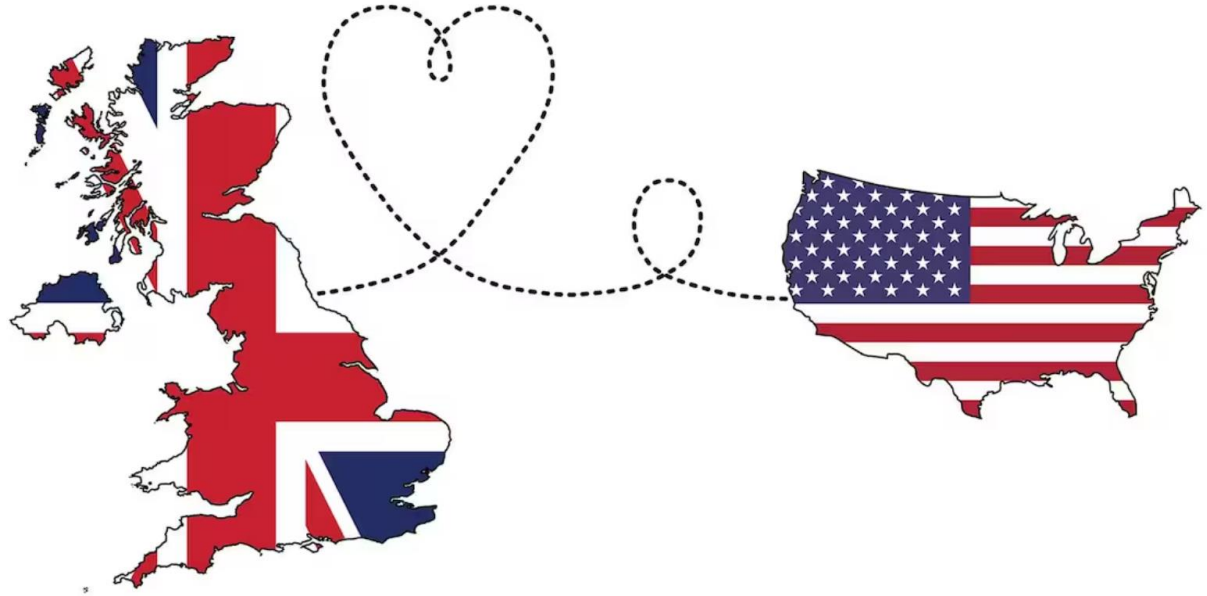
Sealed envelopes at sites

- ***Varying block size***
- ***Stratified by centre***

Open label

UK & USA

26 Major Trauma Centres



CRYOSTAT-2 METHODS:

Sample Size:

Aim to detect an absolute mortality difference of 7%
Baseline mortality 26%. 90% power

1568 with predicted 2.5% drop-outs
Adjusted to 1600 with observed 4.4% drop-out

Analysis on ITT basis, including all randomized participants

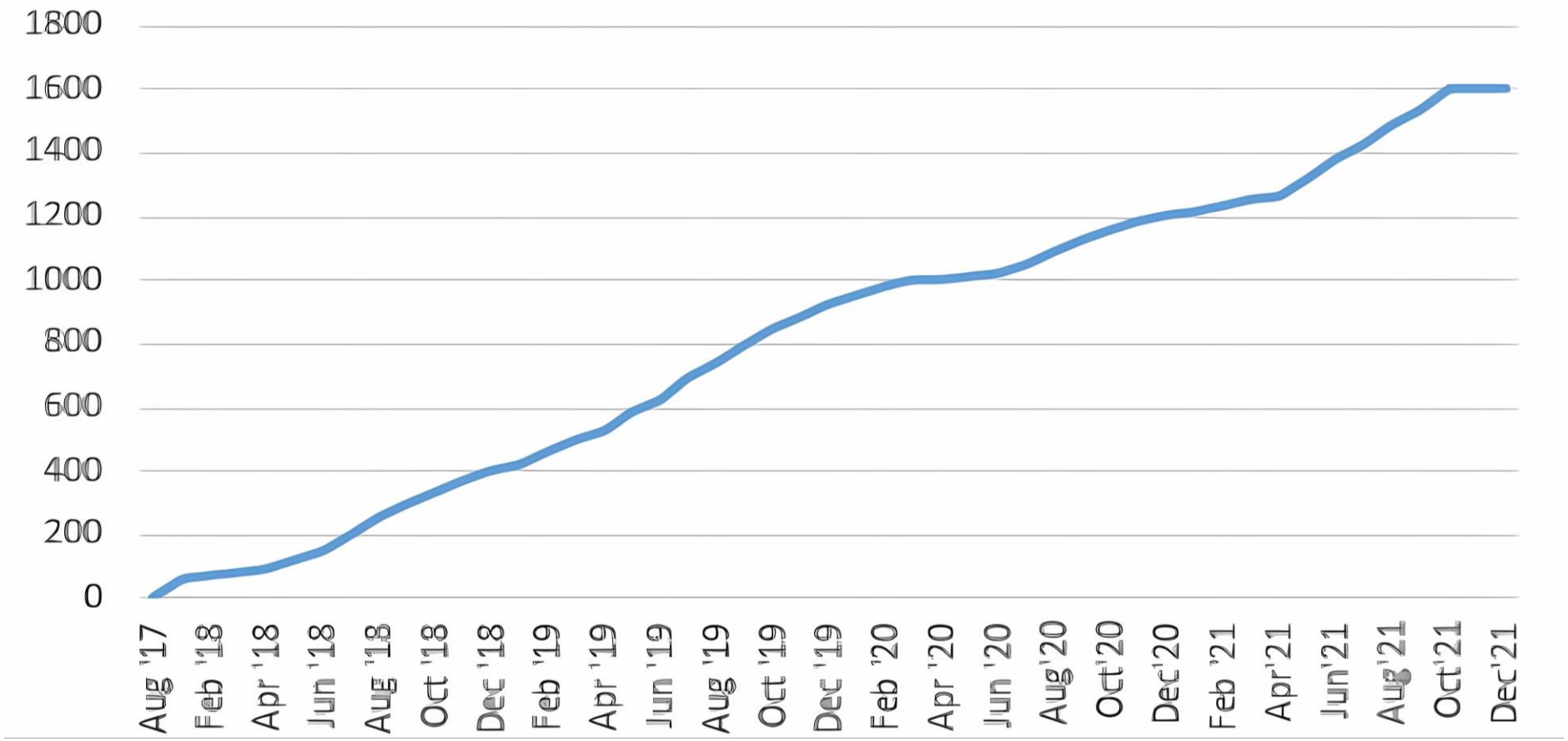
Prespecified Subgroups:

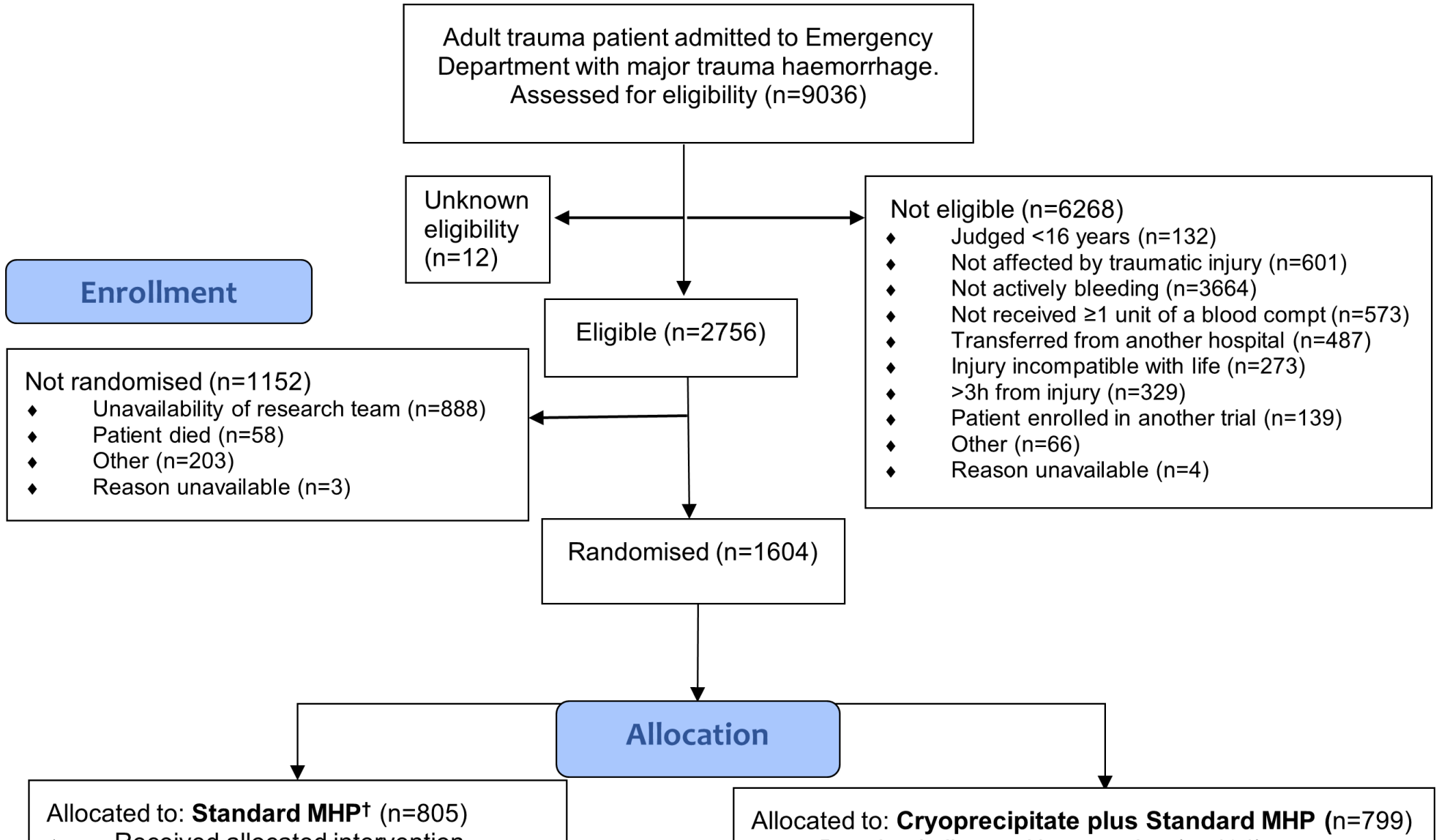
Per protocol, Time to Cryo, Sex, Age, TBI, Mechanism, Country


A
Cryoprecipitate (CPD-A1)
Human
A
Rh-POSITIVE
Cryoprecipitate (CPD-A1)
Human
Lot 87K04867
DO NOT USE
17 APR 1903
A

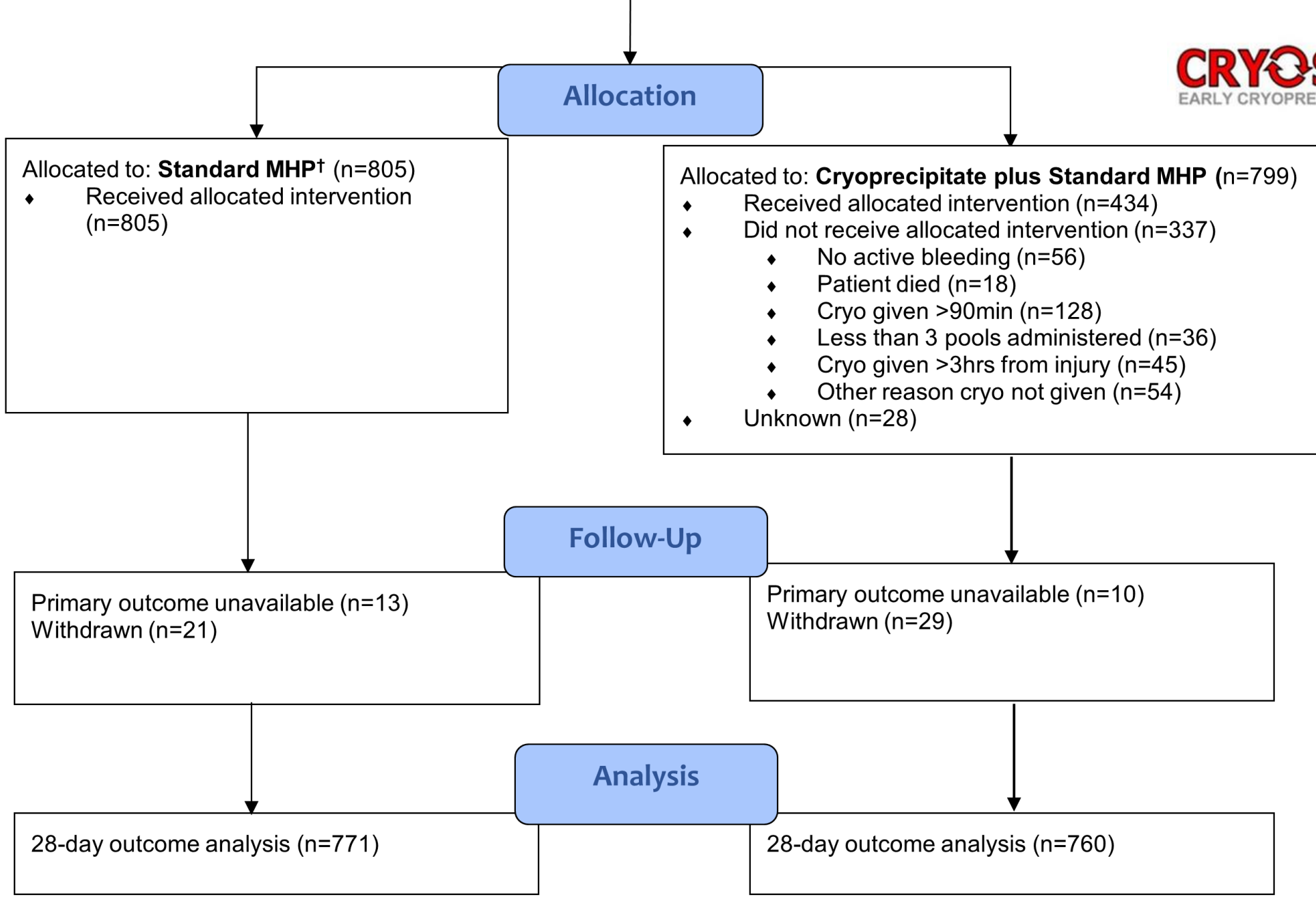
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

CRYOSTAT-2 Recruitment




Adult trauma patient admitted to Emergency Department with major trauma haemorrhage. Assessed for eligibility (n=9036)
Unknown eligibility (n=12)
Not eligible (n=6268)
Judged <16 years (n=132)
Not affected by traumatic injury (n=601)
Not actively bleeding (n=3664)
Not received ≥1 unit of a blood compt (n=573)
Transferred from another hospital (n=487)
Injury incompatible with life (n=273)
>3h from injury (n=329)
Patient enrolled in another trial (n=139)
Other (n=66)
Reason unavailable (n=4)
Enrollment
Eligible (n=2756)
Not randomised (n=1152)
Unavailability of research team (n=888)
Patient died (n=58)
Other (n=203)
Reason unavailable (n=3)
Randomised (n=1604)
Allocation
Allocated to: Standard MHP† (n=805)
Allocated to: Cryoprecipitate plus Standard MHP (n=799)

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA



CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Patient characteristics

	Std MHP (n=805)	*Early Cryo (n=799)*
Male	*80%*	*79%*
Age (years)	*40 (26-55)*	*38 (25-55)*
Time from injury to ED (mins)	*77 (55-100)*	*75 (55-99)*
Penetrating injury	*35%*	*37%*
Injury Severity score	*29 (18-43)*	*29 (17-43)*
Systolic blood pressure (mm Hg)	*103 (83-126)*	*102 (84-124)*
Glasgow Coma Scale score	*13 (3-15)*	*14 (3-15)*

Prehospital Care

	Std MHP (n=805)	*Early Cryo (n=799)*
RBC units	*0 (0-2)*	*0 (0-2)*
FFP units	*0 (0-1)*	*0 (0-1)*
Crystalloid (mls)	*0 (0-250)*	*0 (0-250)*
TXA	*80%*	*79%*

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome: All cause 28-day mortality

	Std MHP	*Early Cryo*
28-day Mortality	***26.1%***	***25.3%***
		OR: 0.96 (0.75-1.23)
Missing primary outcome	***4.2%***	***4.9%***

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Secondary Outcomes: 6 & 24 hr Mortality

	Std MHP	*Early Cryo*	
6-hr mortality	*8.6%*	*7.1%*	*0.82 (0.61 – 1.15)*
24-hr mortality	*12.2%*	*11.2%*	*0.91 (0.63 – 1.31)*
6-hr deaths from bleeding	*4.4%*	*4.1%*	*0.93 (0.54 – 1.58)*
24-hr deaths from bleeding	*4.9%*	*5.5%*	*1.13 (0.62 – 2.05)*
Time to death from bleeding (mins)	*86 (40-205)*	*191 (81-445)*	

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Secondary Outcomes: Transfusion requirements
Injury to 24 hours

	Std MHP	*Early Cryo*
RBC units	*5 (3-8)*	*5 (3-9)*
FFP	*4 (2-8)*	*4 (2-8)*
Platelets	*0 (0-1)*	*0 (0-1)*
Cryoprecipitate	*0 (0-2)*	*3 (3-3)*
Crystalloid (mls)	*1600 (250-3200)*	*2000 (700-3500)*

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

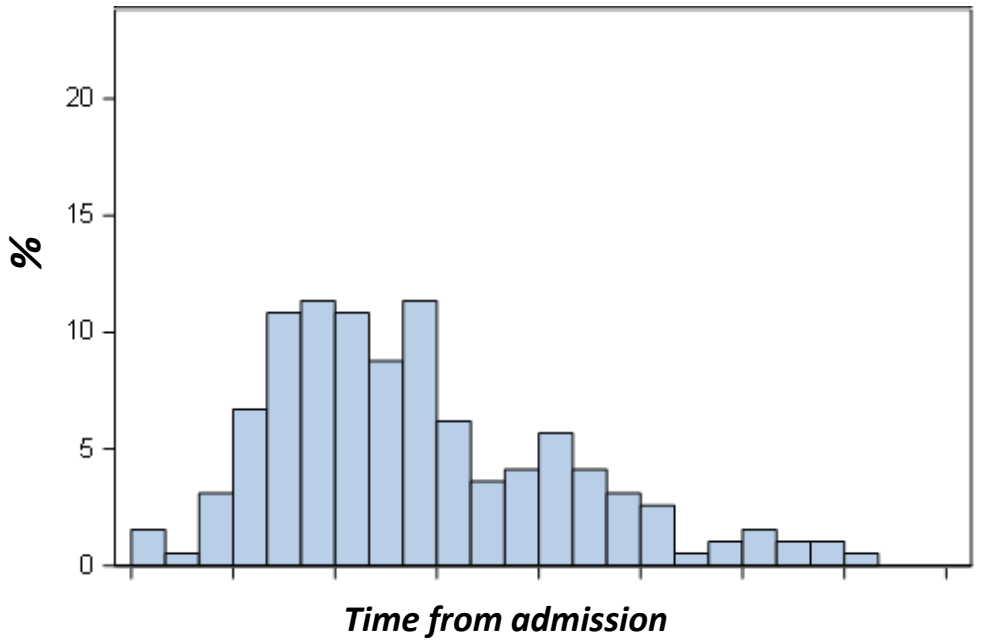
Secondary Outcomes: Complications & Safety

	Std MHP	*Early Cryo*
Thrombotic events		
Venous	***7.1%***	***6.9%***
Arterial	***3.2%***	***3.3%***
Transfusion related events	***0.0%***	***0.4%***

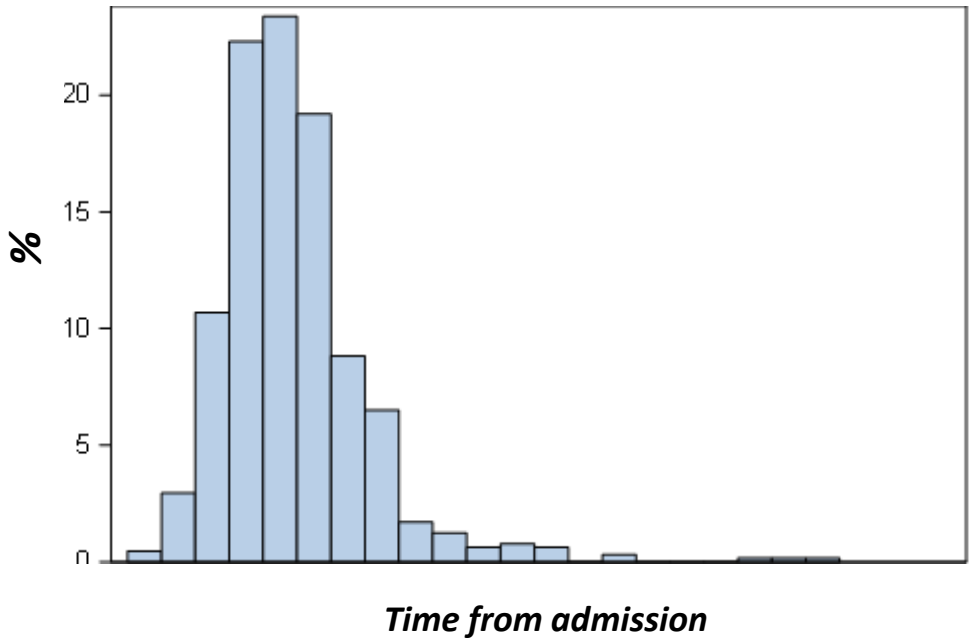
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Timing of Cryoprecipitate

Std MHP



Cryo

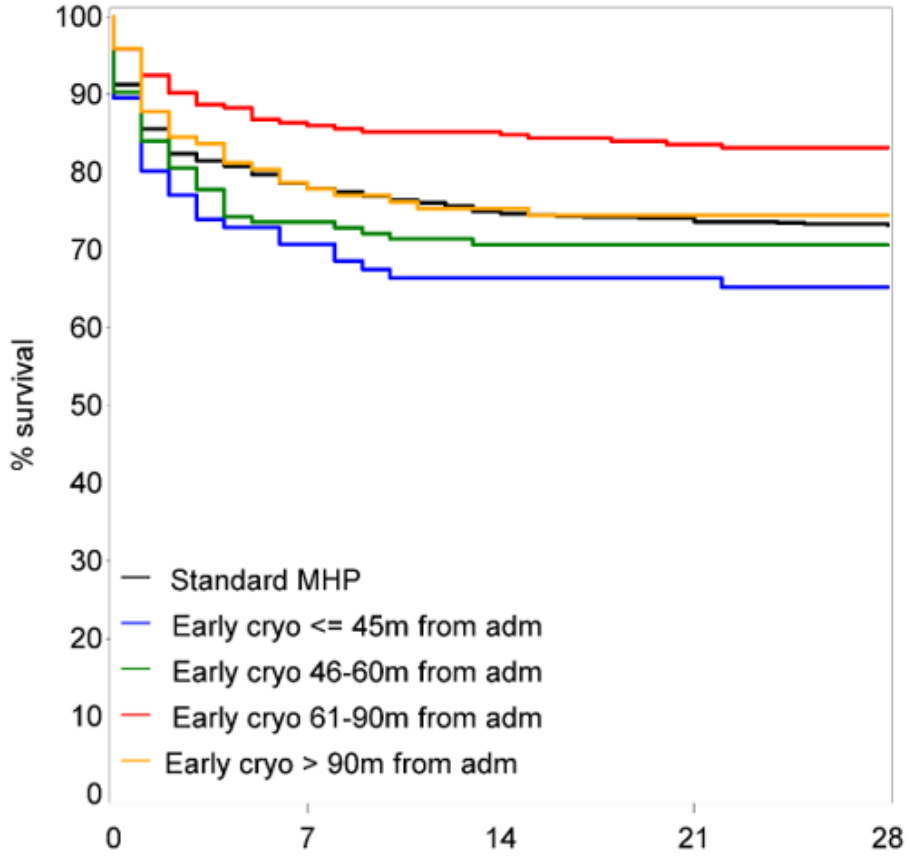


Median time to Cryo: 120 (79-184) vs 68 (53-85) mins

% Cryo within 90 mins: 9% vs 68%

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

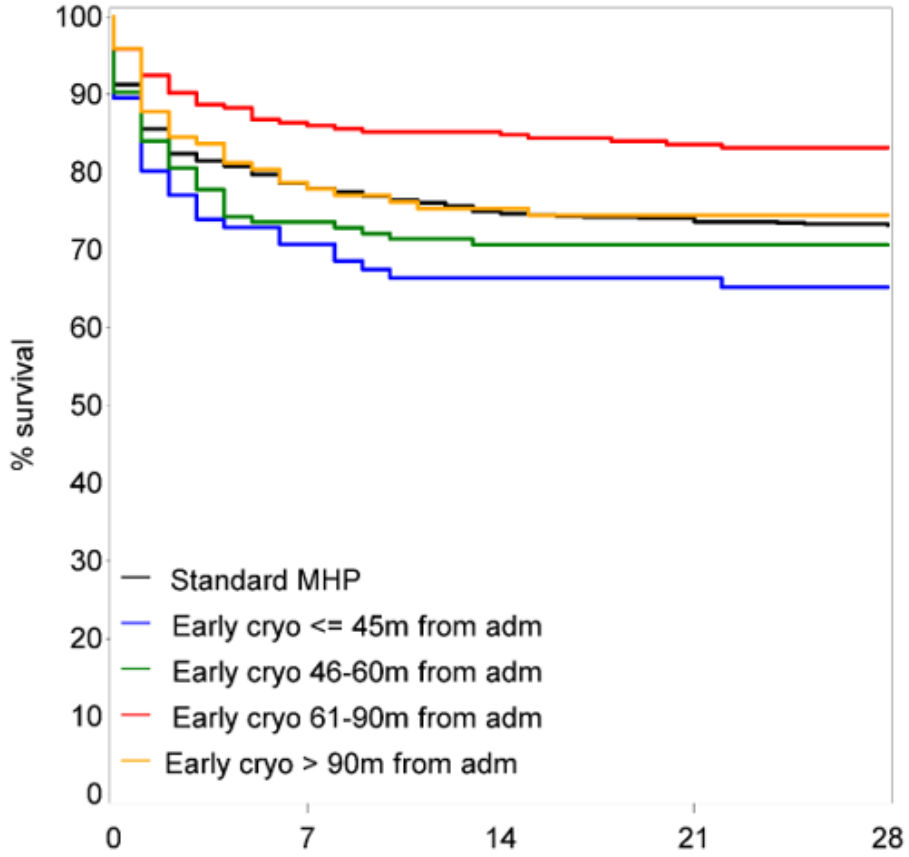
Primary Outcome by timing of Cryoprecipitate



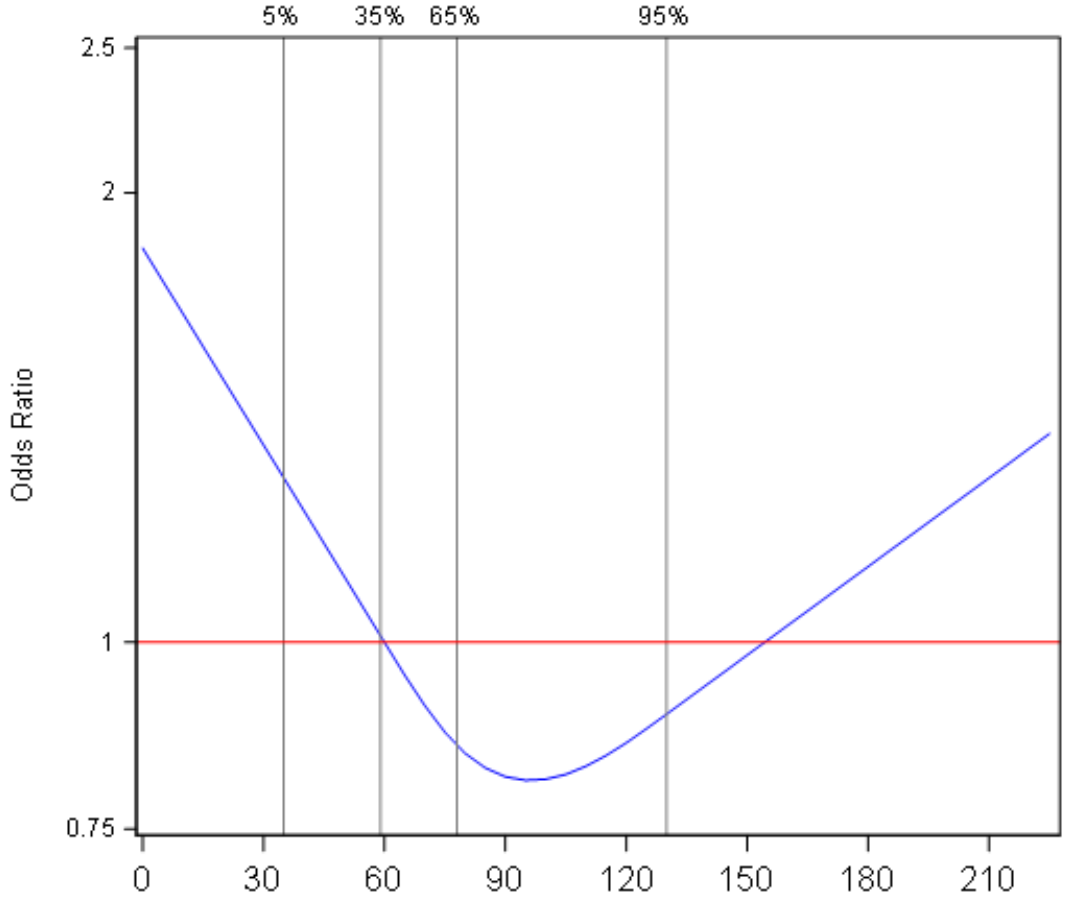
Days since admission

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by timing of Cryoprecipitate



Days since admission



Timing of Cryo Administration

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EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by timing of Cryoprecipitate

	Std MHP	Cryo <45 mins	Cryo 46-60 mins	Cryo 60-90 mins	Cryo >90 mins
n	805	101	147	273	128
28-day Mortality	*26.1%*	*34.4%*	*29.2%*	*16.5%*	*25.2%*
OR		*1.29 (0.94-1.77)*	*1.11 (0.84-1.48)*	*0.65 (0.46-0.91)*	*1.00 (0.71-1.41)*

CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

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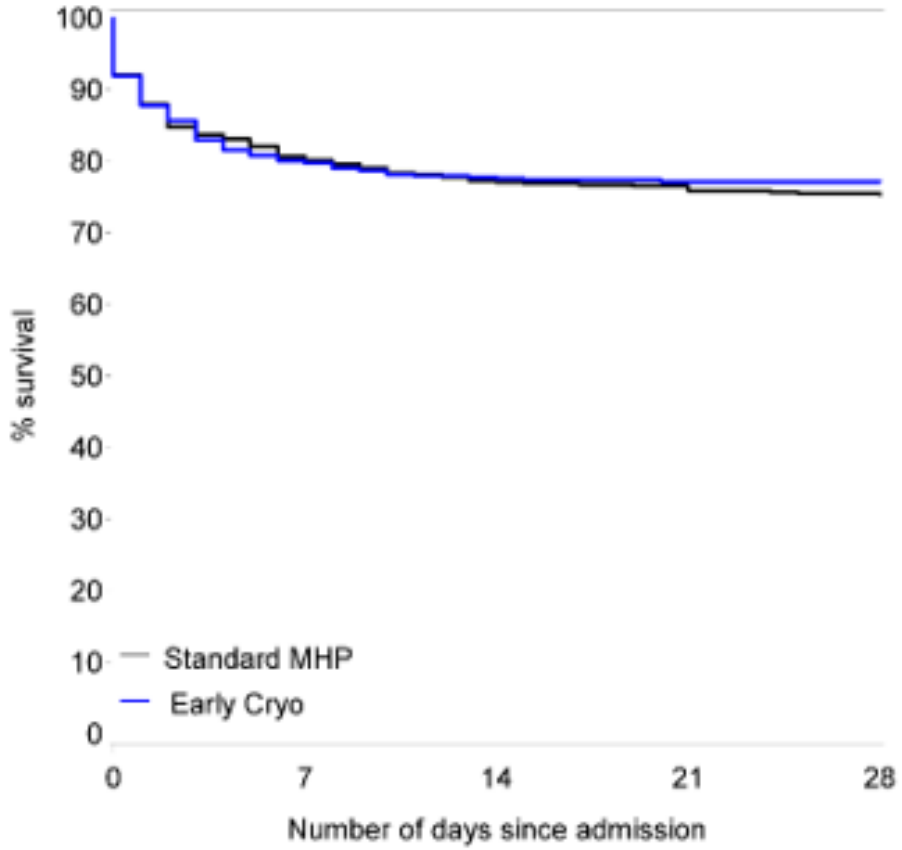
28-day Mortality	*26.1%*	*34.4%*	*29.2%*	*16.5%*	*25.2%*
OR		*1.29 (0.94-1.77)*	*1.11 (0.84-1.48)*	*0.65 (0.46-0.91)*	*1.00 (0.71-1.41)*
Penetrating	*35%*	*41%*	*41%*	*36%*	*36%*
ISS	*29*	*33*	*29*	*29*	*29*
SBP	*103 (83-126)*	*98 (78-121)*	*104 (80-126)*	*99 (84-122)*	*104 (84-126)*

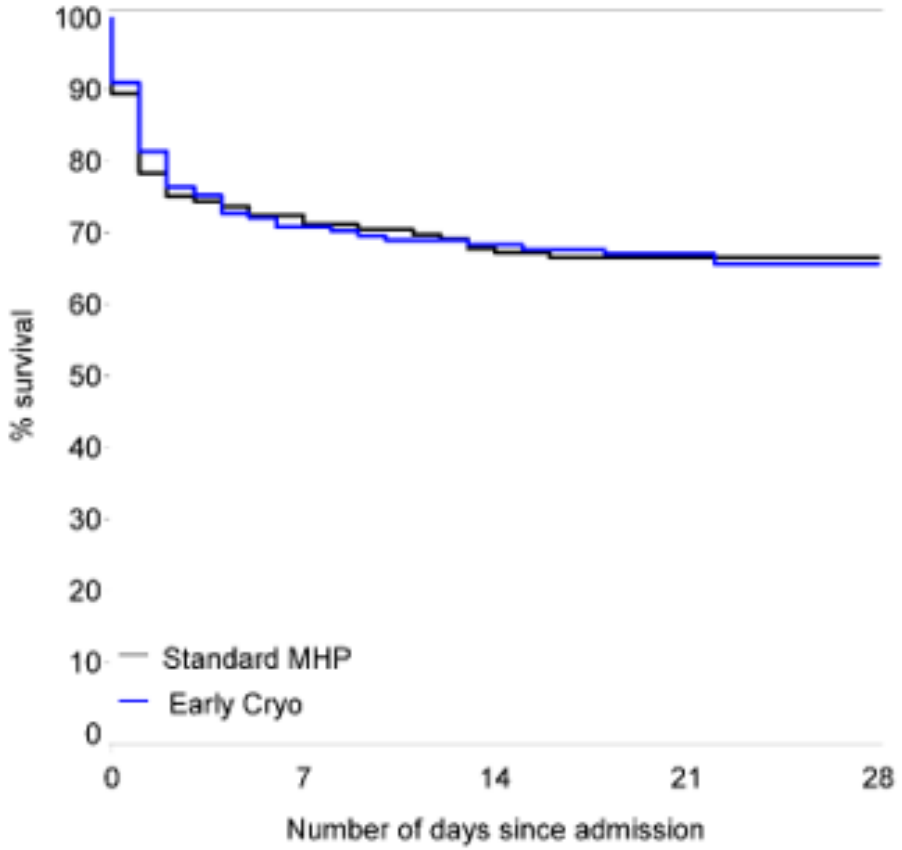
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by Subgroup

Male



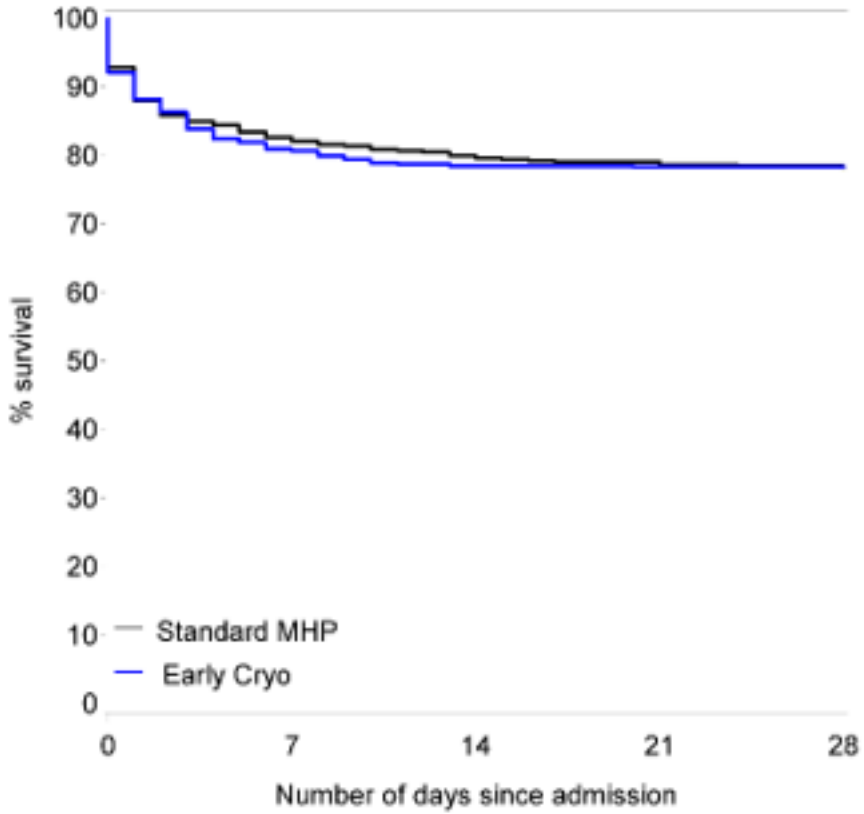
Female



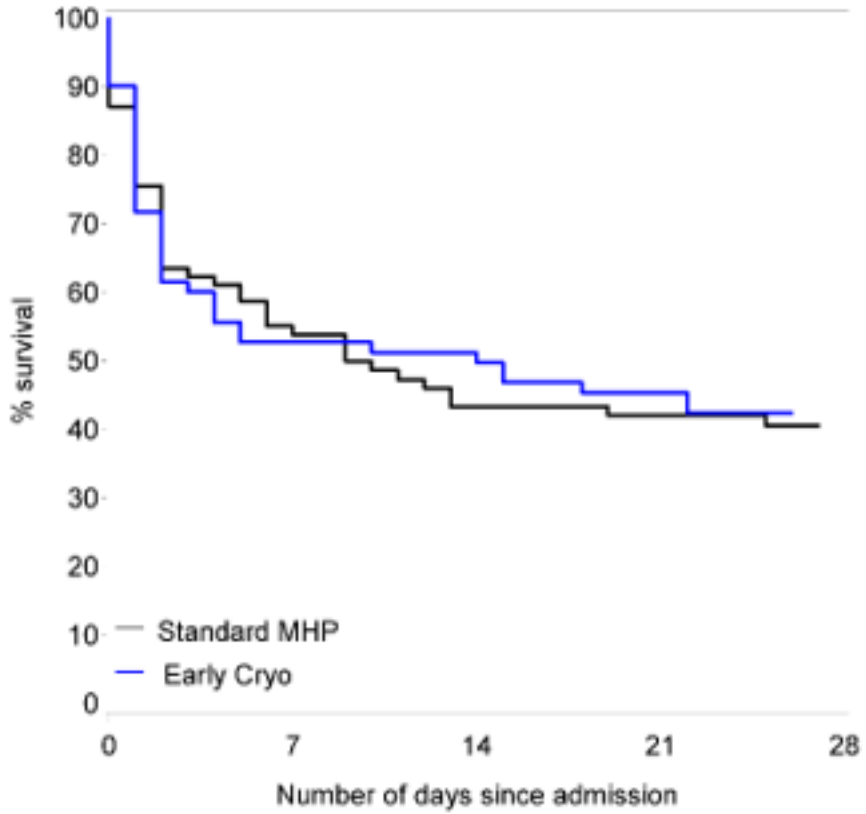
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by Subgroup: Age

Age <70 years



Age 70+ years



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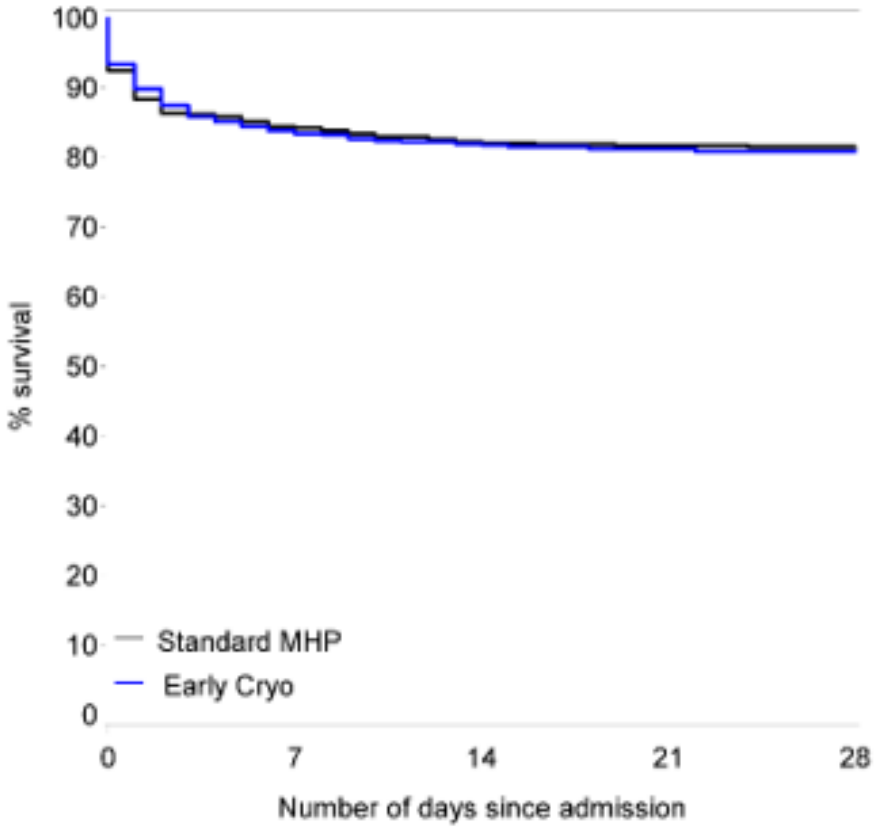
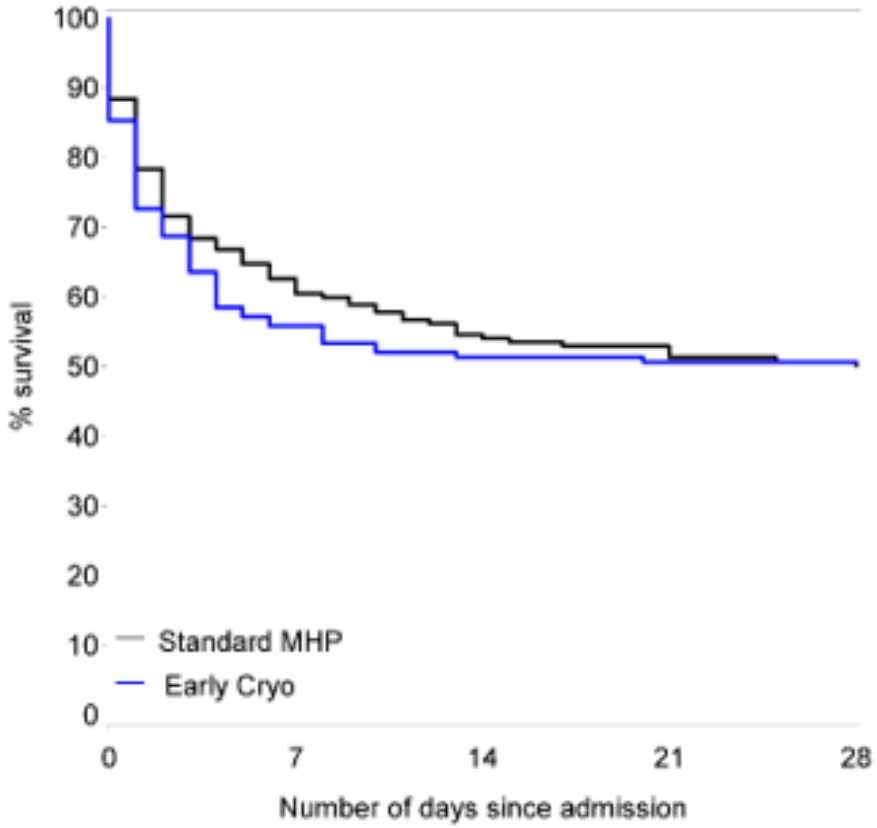
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by Subgroup: TBI

Head AIS <4



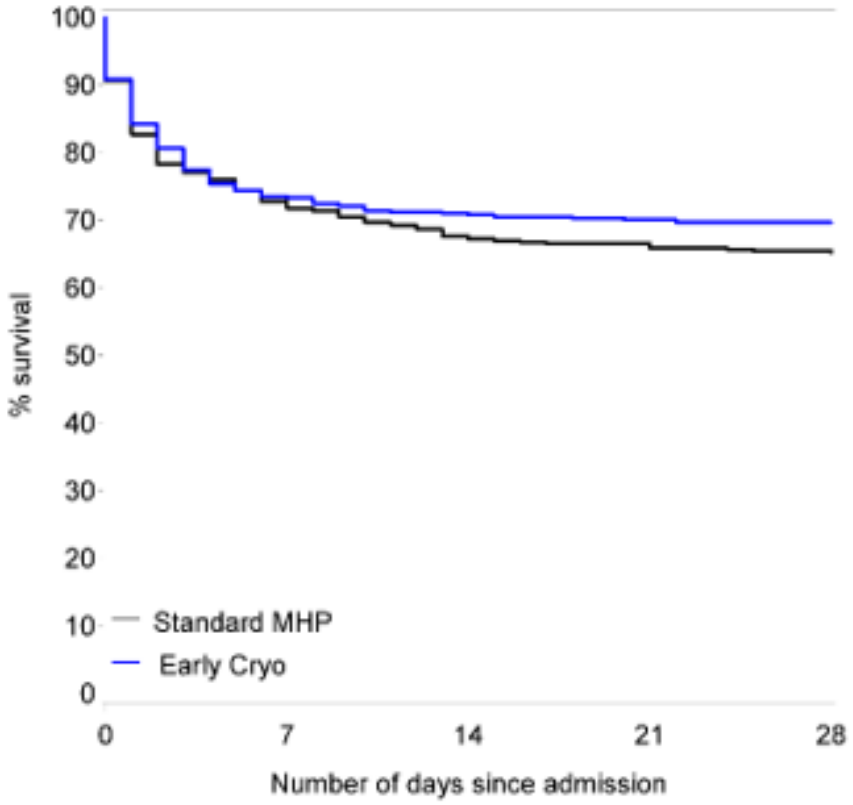
Head AIS 4+



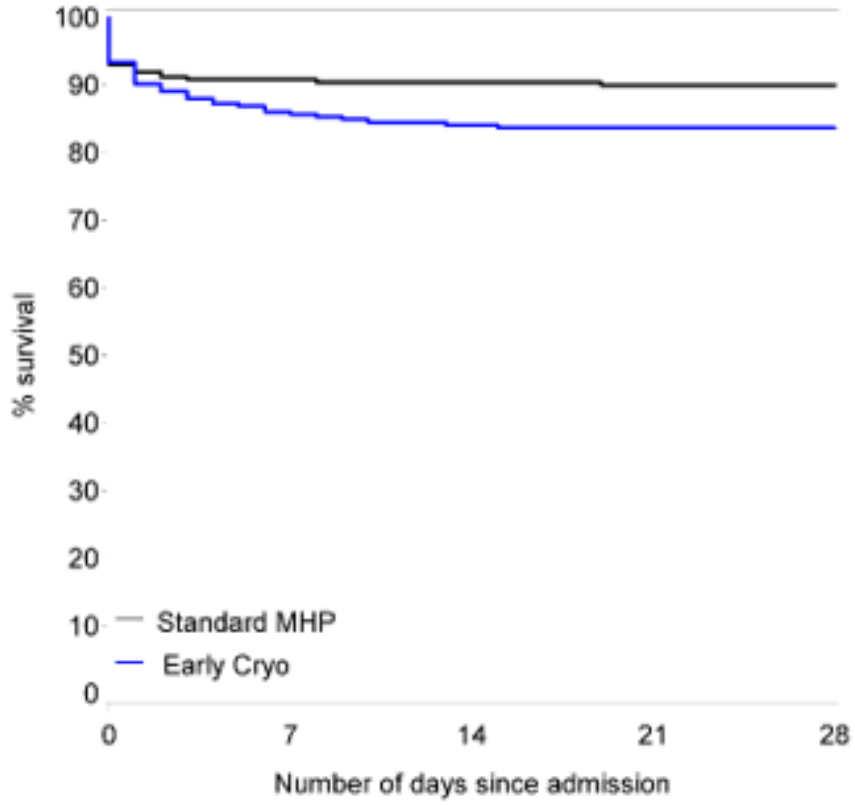
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by Subgroup: Mechanism

Blunt



Penetrating



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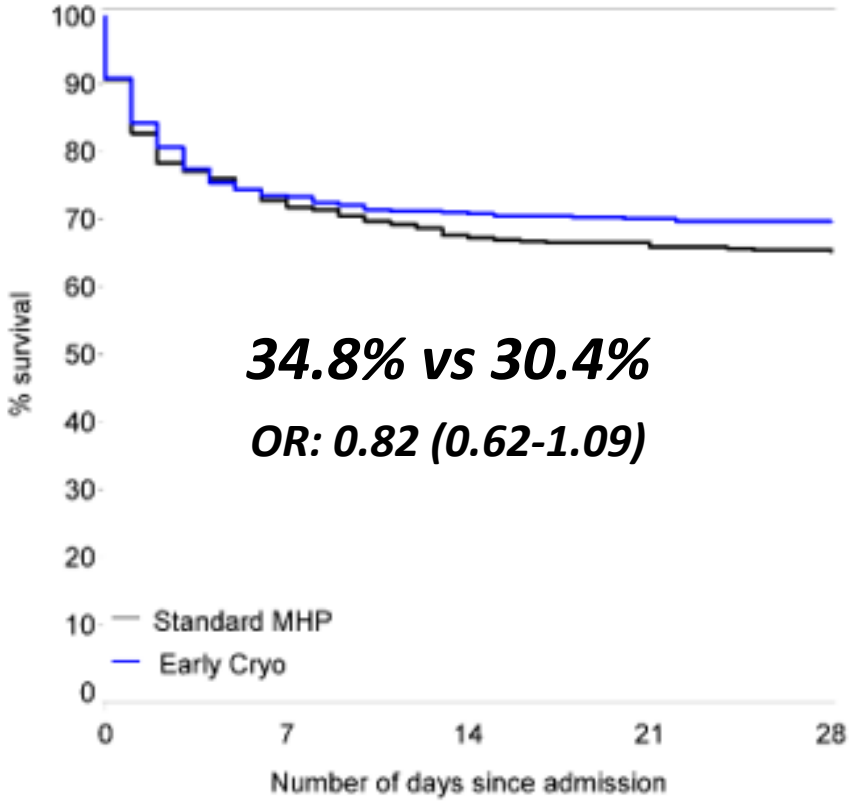
Primary Outcome by Subgroup: Mechanism

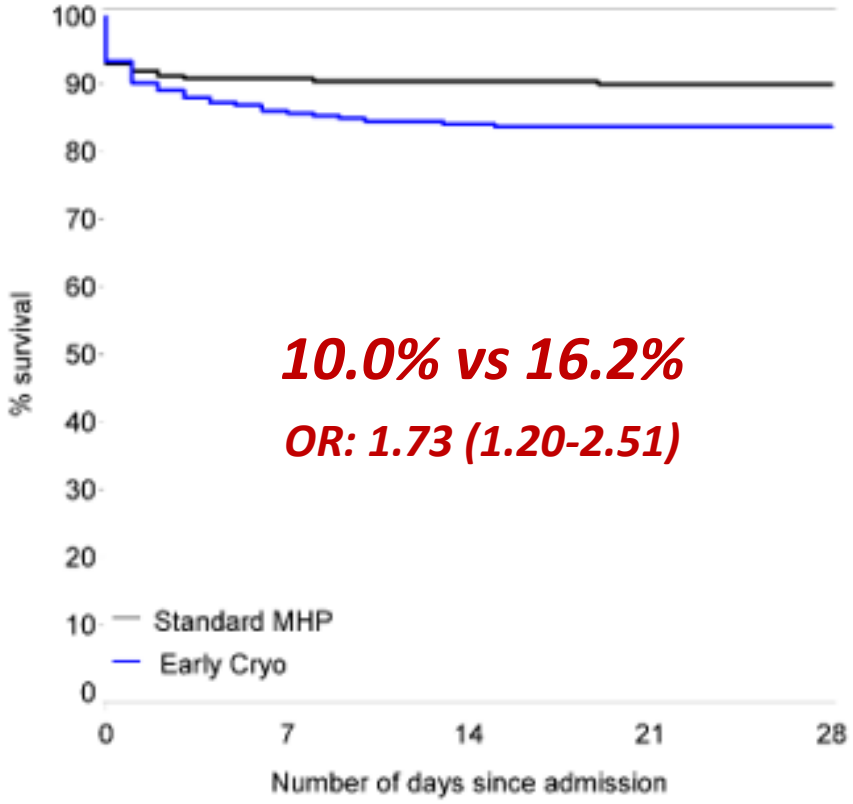
Blunt



34.8% vs 30.4%

OR: 0.82 (0.62-1.09)

Penetrating



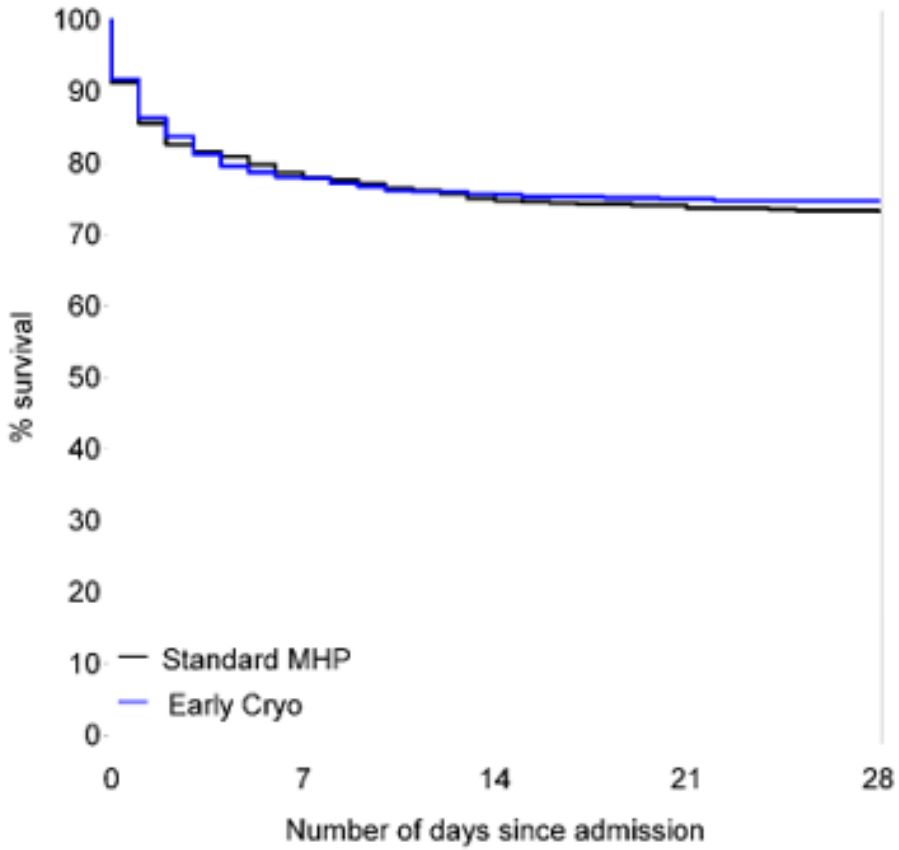
10.0% vs 16.2%

OR: 1.73 (1.20-2.51)

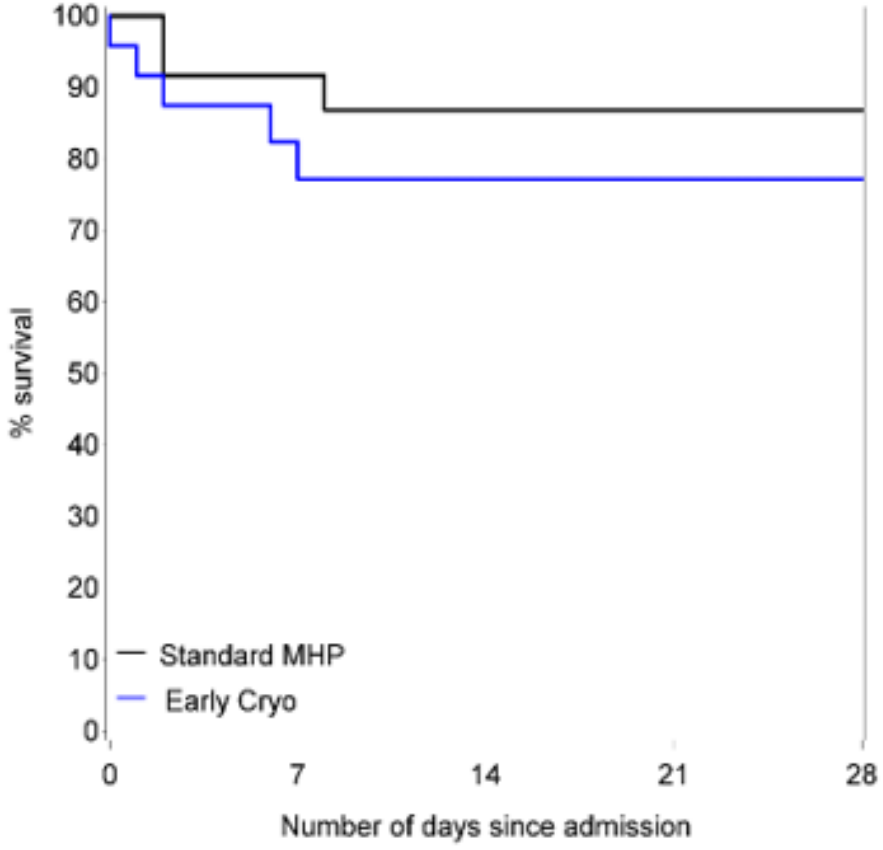
CRYOSTAT-2
EARLY CRYOPRECIPITATE IN TRAUMA

Primary Outcome by Subgroup: Country

UK



US



CRYOSTAT-2
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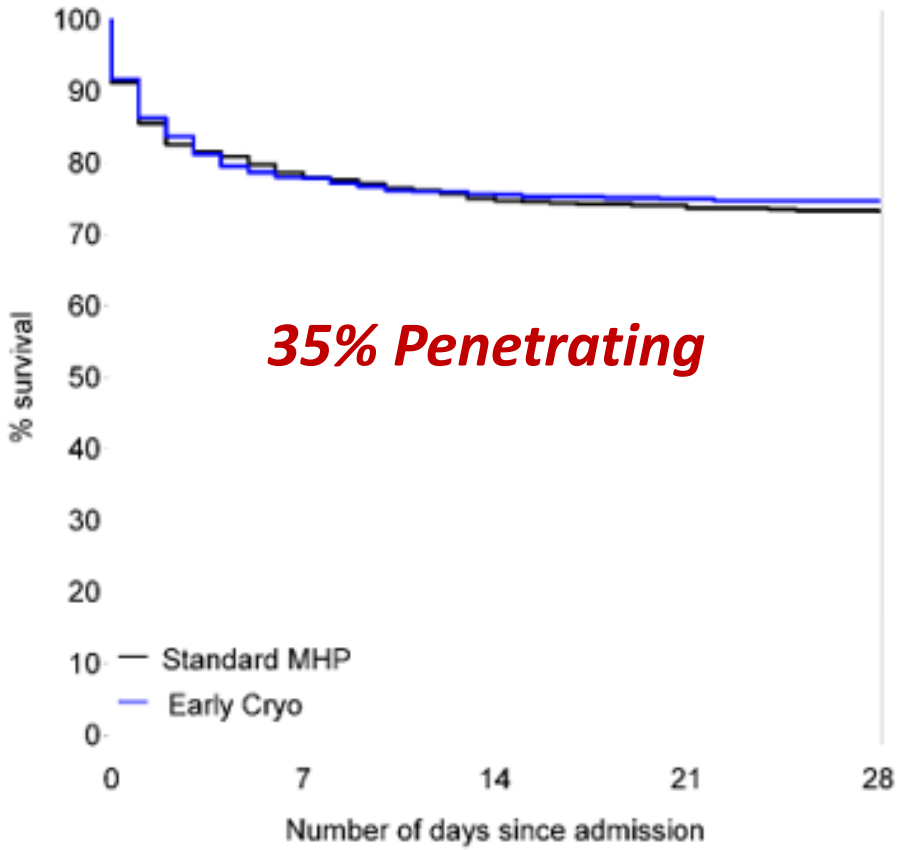
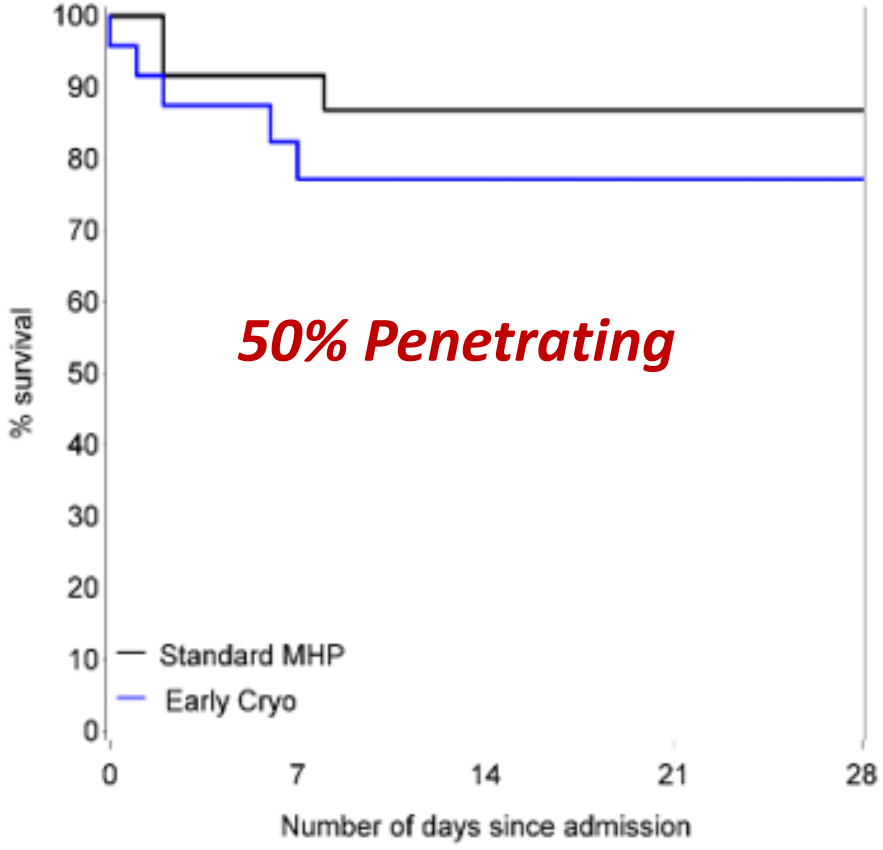
Primary Outcome by Subgroup: Country

UK



35% Penetrating

US



50% Penetrating

CRYOSTAT-2

EARLY CRYOPRECIPITATE IN TRAUMA

Early, empiric, administration of high-dose cryoprecipitate did not improve 28-day mortality in severe trauma haemorrhage