Cold Stored Platelet Trials
in Hemorrhagic Shock

The CriSP-HS

Multi-center and Single-center, Prospective, Randomized Clinical Trials

J. Sperry, F. Guyette, S. Wisniewski, B. Rosario-Rivera, M. Kutcher, L. Kornblith, B. Cotton, C. Wilson, K. Inaba, E Zadorozny, L. Vincent, A. Harner, E. Love, M. Neal, D. Okonkwo, A. Puccio, M. Yazer, J. Luther and CriSP study groups

THOR 2024
Miami, FL
OCT 6th-9th

Pitt

LiTES

Disclosures

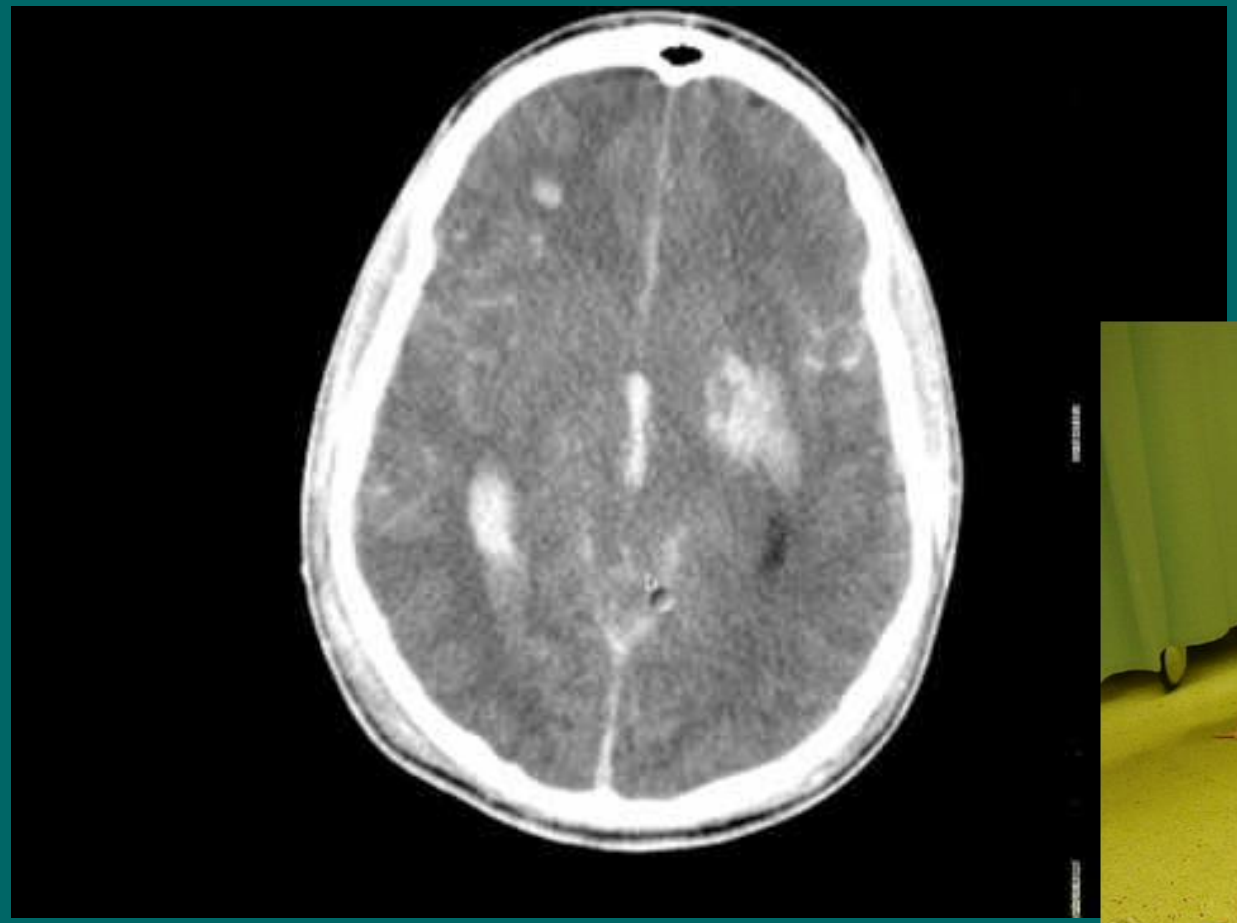
- No conflicts to report.

- FUNDING

- **This research is supported by DoD Contract No. W81XWH-16-D-0024, Task Order W81XWH-19-F-0494.**

- **Any opinions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the Department of Defense.**

Traumatic Injury Morbidity/Mortality



PROPPR and Platelets in HS

Research

Original Investigation

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma The PROPPR Randomized Clinical Trial

REGULAR ARTICLE

blood advances

Platelet transfusions improve hemostasis and survival in a substudy of the prospective, randomized PROPPR trial

Jessica C. Cardenas,[1,2] Xu Zhang,[3] Erin E. Fox,[1-3] Bryan A. Cotton,[1-3] John R. Hess,[4] Martin A. Schreiber,[5] Charles E. Wade,[1-3] and John B. Holcomb,[1-3] on behalf of the PROPPR Study Group

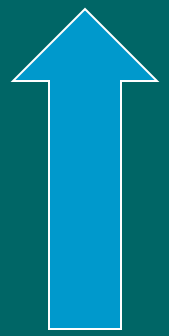
[1]Division of Acute Care Surgery, Department of Surgery, McGovern School of Medicine, [2]Center for Translational Injury Research, and [3]Center for Translational and Clinical Studies, University of Texas Health Science Center, Houston, TX; [4]Department of Laboratory Medicine, Harborview Medical Center, University of Washington, Seattle, WA; and [5]Division of Trauma, Critical Care and Acute Care Surgery, Department of Surgery, Oregon Health and Science University, Portland, OR

Shelf Life and Supply-Austere Environments

Cold vs RT platelets

Reduced Infectious Risk

5 days to 14 days



Supply Available

Received: 30 June 2023 | Revised: 14 September 2023 | Accepted: 21 September 2023
DOI: 10.1111/trf.17572

HOW DO I DO IT

TRANSFUSION

How do I manage a blood product shortage?

Richard Gammon[1] | Joanne Becker[2] | Tracy Cameron[3] | Quentin Eichbaum[4] | Aikaj Jindal[5] | Divjot Singh Lamba[6] | Shaughn Nalezinski[7] | Jorge Rios[8] | Salima Shaikh[9] | Janine Shepherd[10] | Yvette C. Tanhehco[11]

Alternative Procedures for the Manufacture of Cold-Stored Platelets Intended for the Treatment of Active Bleeding when Conventional Platelets Are Not Available or Their Use Is Not Practical

Guidance for Industry

This guidance is for immediate implementation.

June 2023

Early Better

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 26, 2018 VOL. 379 NO. 4

Prehospital Plasma during Air Medical Transport in Trau Patients at Risk for Hemorrhagic Shock

J.L. Sperry, F.X. Guyette, J.B. Brown, M.H. Yazer, D.J. Triulzi, B.J. Early-Young, P.W. Adams, B.J. Daley, R.S B.G. Harbrecht, J.A. Claridge, H.A. Phelan, W.R. Witham, A.T. Putnam, T.M. Duane, L.H. Alarcon, C.W. C B.S. Zuckerbraun, M.D. Neal, M.R. Rosengart, R.M. Forsythe, T.R. Billiar, D.M. Yealy, A.B. Peitzma and M.S. Zenati, for the PAMPer Study Group*

Research

JAMA Surgery | Original Investigation

Tranexamic Acid During Prehospital Transport in Patients at Risk for Hemorrhage After Injury A Double-blind, Placebo-Controlled, Randomized Clinical Trial

Francis X. Guyette, MD, MPH; Joshua B. Brown, MD, MSc; Mazen S. Zenati, MD, PhD; Barbara J. Early-Young, BSN; Peter W. Adams, BS; Brian J. Eastridge, MD; Raminder Nirula, MD, MPH; Gary A. Vercruysse, MD; Terence O'Keeffe, MD; Bellal Joseph, MD; Louis H. Alarcon, MD; Clifton W. Callaway, MD, PhD; Brian S. Zuckerbraun, MD; Matthew D. Neal, MD; Raquel M. Forsythe, MD; Matthew R. Rosengart, MD, MPH; Timothy R. Billiar, MD; Donald M. Yealy, MD; Andrew B. Peitzman, MD; Jason L. Sperry, MD, MPH; and the STAAMP Study Group

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prehospital Tranexamic Acid for Severe Trauma

The PATCH-Traur

Research

JAMA | Original Investigation

Effect of Out-of-Hospital Tranexamic Acid vs Placebo on 6-Month Functional Neurologic Outcomes in Patients With Moderate or Severe Traumatic Brain Injury

Susan E. Rowell, MD, MBA; Eric N. Meier, MS; Barbara McKnight, PhD; Delores Kannas, RN, MS, MHA; Susanne May, PhD; Kellie Sheehan, RN; Eileen M. Bulger, MD; Ahamed H. Idris, MD; Jim Christenson, MD; Laurie J. Morrison, MD; Ralph J. Frascone, MD; Patrick L. Bosarge, MD; M. Riccardo Colella, DO, MPH; Jay Johannigman, MD; Bryan A. Cotton, MD; Jeannie Callum, MD; Jason McMullan, MD; David J. Dries, MD;); Martin D. Zielinski, MD; MD, MPH; Lauren Klein, MD, MS; liams, RN; Audrey Hendrickson, MPH; n A. Schreiber, MD

2021 AAST Quick Shot

Prehospital low titer group O whole blood is feasible and safe: Results of a prospective randomized pilot trial

Frank X. Guyette, MD, MPH, Mazen Zenati, MD, PhD, Darrell J. Triulzi, MD, Mark H. Yazer, MD, Hunter Skroczky, BS, Barbara J. Early, BSN, Peter W. Adams, BS, Joshua B. Brown, MD, MCS, Louis Alarcon, MD, Matthew D. Neal, MD, Raquel M. Forsythe, MD, Brian S. Zuckerbraun, MD, Andrew B. Peitzman, MD, Timothy R. Billiar, MD, *and* **Jason L. Sperry, MD, MPH**, *Pittsburgh, Pennsylvania*

Cold Better-Robust

REVIEW

The effect of platelet storage temperature on haemostatic, immune, and endothelial function: potential for personalised medicine

bjh research paper

Platelets stored at 4°C contribute to superior clot properties compared to current standard-of-care through fibrin-crosslinking

SHOCK, Vol. 41, Supplement 1, pp. 54–61, 2014

HEMOSTATIC FUNCTION OF APHERESIS PLATELETS STORED AT 4°C AND 22°C

Kristin M. Reddoch,* Heather F. Pidcoke,† Robbie K. Montgomery,† Chriselda G. Fedyk,† James K. Aden,† Anand K. Ramasubramanian,* and Andrew P. Cap†

SHOCK, Vol. 41, Supplement 1, pp. 51–53, 2014

Review Article

REFRIGERATED PLATELETS FOR THE TREATMENT OF ACUTE BLEEDING: A REVIEW OF THE LITERATURE AND REEXAMINATION OF CURRENT STANDARDS

Heather F. Pidcoke,* Philip C. Spinella,† Anand K. Ramasubramanian,‡

SUPPLEMENT ARTICLE

TRANSFUSION

Cold-stored platelets have better preserved contractile function in comparison with room temperature-stored platelets over 21 days

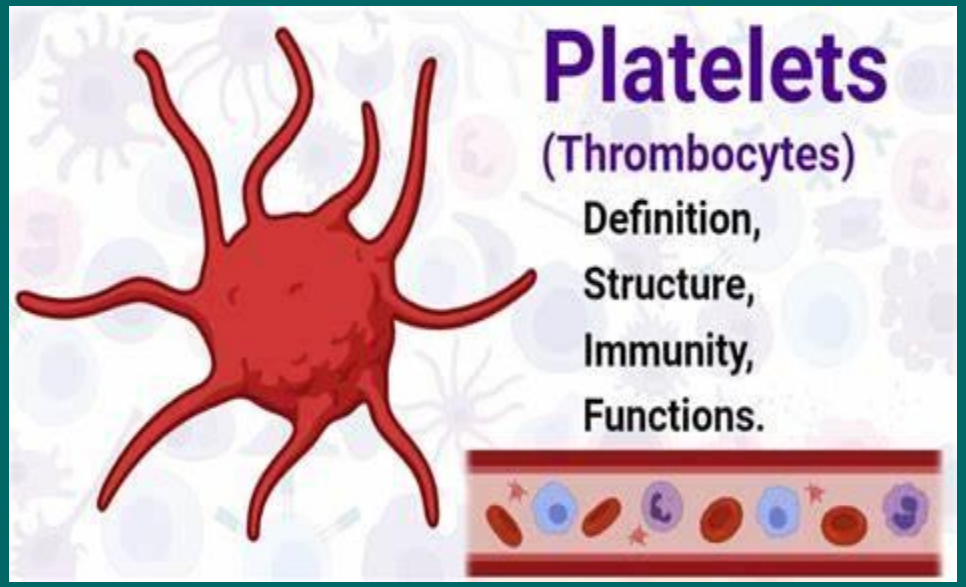
Praj... Xiac... Asw... And...

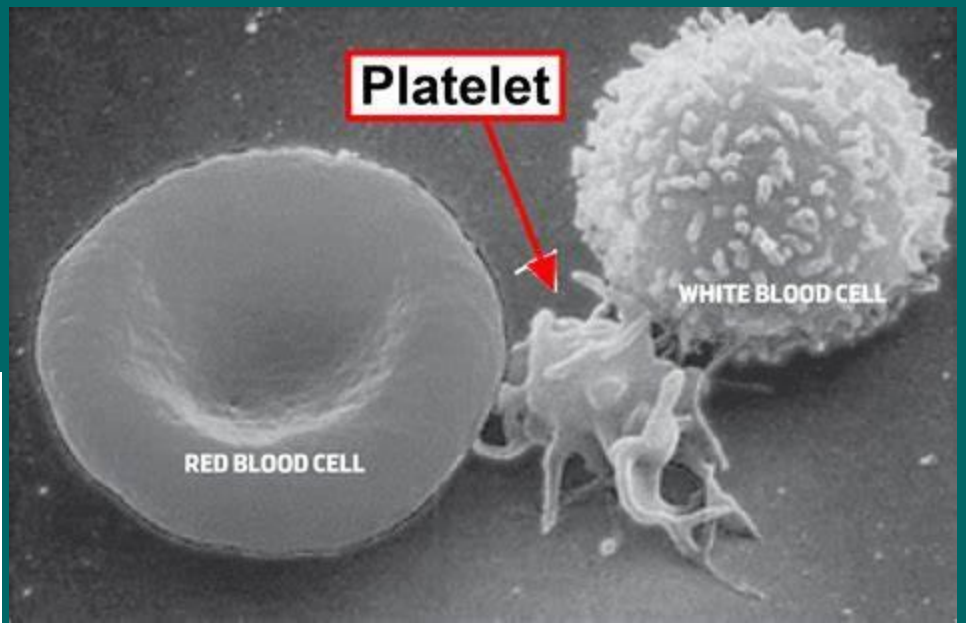
BLOOD COMPONENTS

TRANSFUSION

Cold storage of platelets in platelet additive solution maintains mitochondrial integrity by limiting initiation of apoptosis-mediated pathways

Kristin M. Reddoch-Cardenas[1] | Grant C. Peltier[1] | Tiffani C. Chance[2] | Prajeeda M. Nair[1] | Michael A. Meledeo[1] | Anand K. Ramasubramanian[3] | Andrew P. Cap[1] | James A. Bynum[1]





CriSP-HS Trial

Study Design

Open label, Phase 2, Multi-center, Randomized trial designed to determine the efficacy and safety of incorporating early CSPs into early trauma resuscitation vs. standard of care resuscitation in patients at risk of hemorrhagic shock.

CriSP-HS Trial

Setting

- 3-year planned enrollment
- 5 level 1-trauma centers
- At risk of hemorrhagic shock
- University of Mississippi; University of Texas Houston; University of California, San Francisco; Baylor College of Medicine; University of Southern California, LA

CriSP-HS Trial
Eligibility Criteria

- **Assessment of Blood Consumption Score (ABC):**
  - **SBP <90mmHg; Penetrating mechanism; Positive FAST; HR >120**

AND

- **Hemorrhage control procedure in 60 minutes (OR/IR)**

- **Exclusion:**
- **Wearing "NO CRISP" opt-out bracelet**
- **Age > 90 or <15 years of age**
- **Isolated fall; known prisoner; known pregnancy; Isolated burns**
- **Traumatic arrest with >5 min of CPR without return of vital signs**
- **Brain matter exposed or penetrating brain injury (GSW)**
- **Isolated drowning or hanging victims**
- **Objection to study voiced by subject or family member at the scene**

CriSP-HS Trial

Intervention / Comparison Arms

- *OPEN LABEL*
  - **CSP arm**

- **Single apheresis unit cold stored platelets (1-6 ℃) stored local refrigerator**
  - **Out to 14 days from donation**
  - **Transfused as soon as feasible**
  - **Concomitant standard site resuscitation**

  - **Standard Care arm**

- **Standard care prehospital resuscitation**
  - **No requirement for platelet transfusion**

CriSP-HS Trial

Randomization

- 1:1 ratio random allocation sequence to either CSP arm or standard care arm
- Variable block sizes of 4 to 6; computer random-number generator.
- Assignment envelopes in the trauma bay or proximity to ED
- Study team; randomization cards; sealed envelopes; patient level; in real-time.
- Arm assignment was concealed to outcome assessors

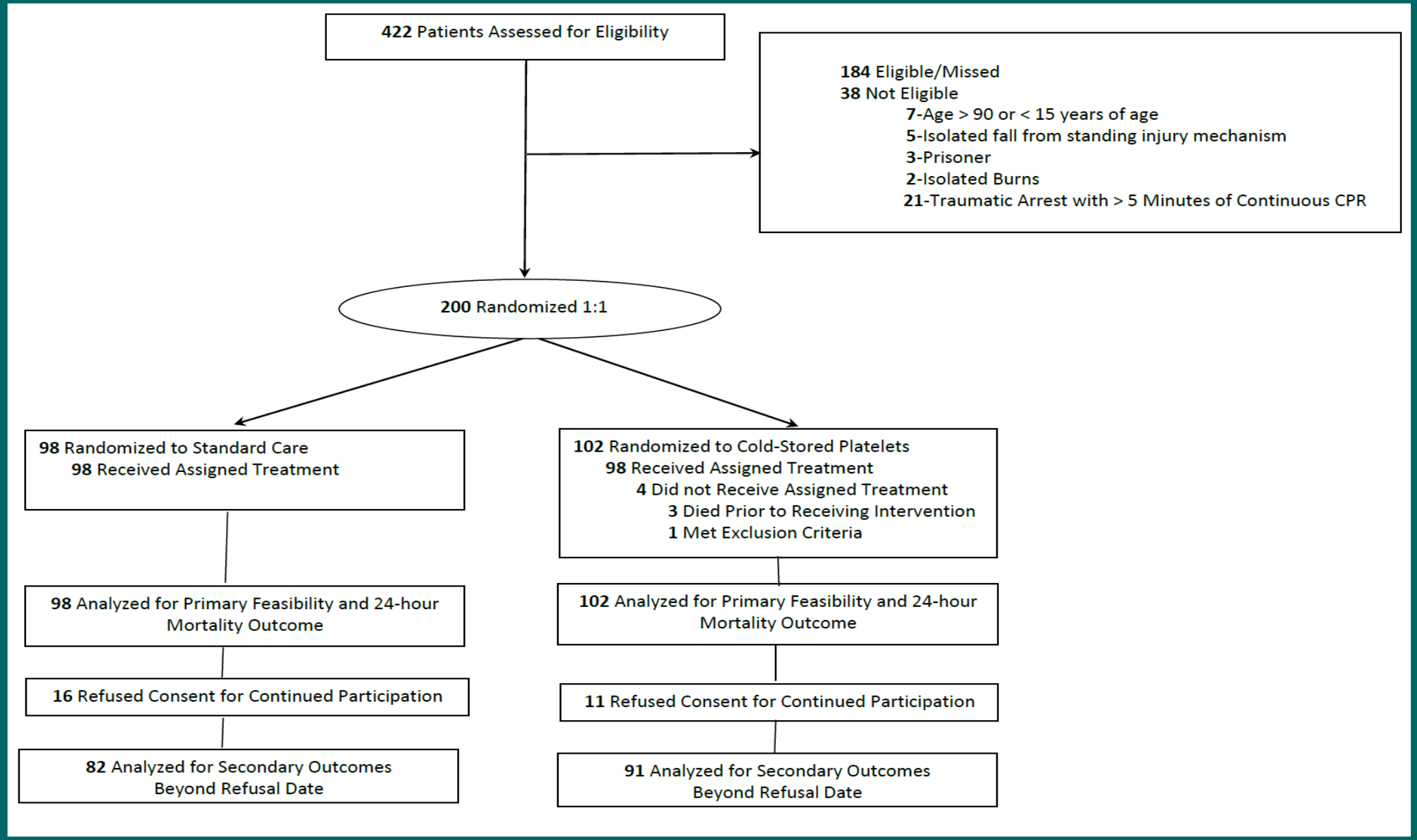
Outcomes

Primary Outcome: Feasibility

Safety / Efficacy: 24-hour mortality

Additional Secondary Outcomes: Mortality time points; death from hemorrhage; time to hemostasis; ARDS; thromboembolic events; coagulation measures, transfusion requirements

CriSP-HS Trial-Enrollment



CriSP-HS Trial-Cohort / Randomization

Enrolled Cohort Characteristics

Age- 34 ± 13 years

Sex- 85% male

ISS- median 17 [9-28]

Mechanism- 78.5% penetrating

24-hour mortality- 8%

30-day mortality

Characteristics	n/N (%) Standard care (N = 98)	Cold stored platelets (N = 102)
Age [mean (SD)]	35.3 (14.4)	34.4 (13.5)
Male sex	78/98 (80)	85/102 (83)
Race		
White	18/98 (18)	28/102 (28)
Black	51/98 (52)	47/102 (47)
Other	13/98 (13)	13/102 (13)
Hispanic	13/98 (13)	20/102 (20)
SBP [median (IQR)] (mm Hg)		
Initial	108.5 (84.5, 129.5)	99 (83, 140)
Highest	122 (102, 144)	127 (98, 148)
Lowest	93.5 (78, 117.5)	90 (78, 127)
HR [median (IQR)] (beats/min)		
Initial	106 (86, 123)	112 (88, 130.5)
Highest	111.5 (93, 130)	116 (96.5, 135)
Lowest	95 (81.5, 117)	101 (75, 123)
Transport mode		
Ground EMS	66/98 (67)	71/102 (70)
Air EMS	24/98 (24)	20/102 (20)
Does not apply†	5/98 (5)	4/102 (4)
Transferred from		
Scene of accident/injury	65/98 (66)	73/102 (72)
Home	4/98 (4)	3/102 (3)
Other hospital	26/98 (26)	19/102 (19)
Mechanism of injury blunt	23/98 (23)	12/102 (12)
Fall	5/98 (5)	2/102 (2)
MVC occupant ejected	3/98 (3)	1/102 (1)
MVC occupant not ejected	6/98 (6)	3/102 (3)
MVC motorcycle	5/98 (5)	3/102 (3)
MVCpedestrian	1/98 (1)	2/102 (2)
Struck by or against	3/98 (3)	1/102 (1)
Mechanism of injury penetrating	76/98 (77)	90/102 (88)
Firearm	53/98 (54)	62 /102 (61)
Impalement	1/98 (1)	1/102 (1)
Stabbing	20/98 (20)	26/102 (25)
Other	2/98 (2)	1/102 (1)
AIS [median (IQR)]		
Head and Neck AIS	0, (0, 0)	0, (0, 0)
Face AIS	0, (0, 0)	0, (0, 0)
Chest AIS	1.5 (0, 3)	0 (0, 3)
Abdomen AIS	3 (0, 4)	2 (0, 4)
External AIS	1 (0, 1)	1 (0, 1)
Extremity AIS	0 (0, 3)	0 (0, 3)
ISS‡ [median (IQR)]	17.5 (10, 29)	17 (9, 27)
TBI	9/98 (9)	6/102 (6)
Prehospital advanced airway§	16/98 (16)	12/102 (12)
Supraglottic airway	2/98 (2)	1/102 (1)
Endotracheal intubation	14/98 (14)	11/102 (11)

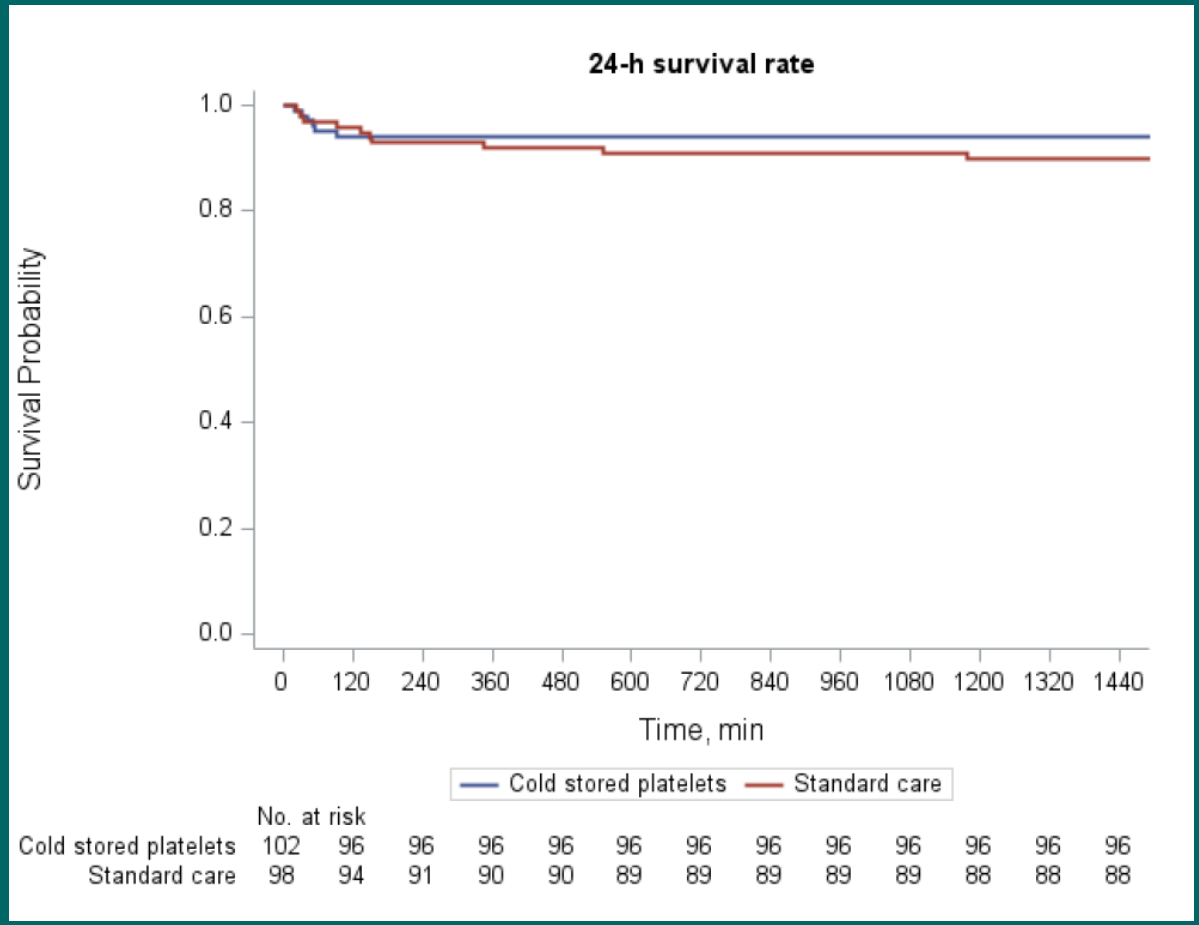
Standard Care Arm: 48% receive platelet transfusion

CriSP-HS Trial-24-hour mortality

CSP 5.9% vs. 10.2%;

Difference -4.3%; 95% CI, -12.8% to 3.5%, P = 0.26

Adjusted for site:
OR 0.6 (95%CI 0.2-1.6)
P=0.27



CriSP-HS Trial-Secondary Outcomes

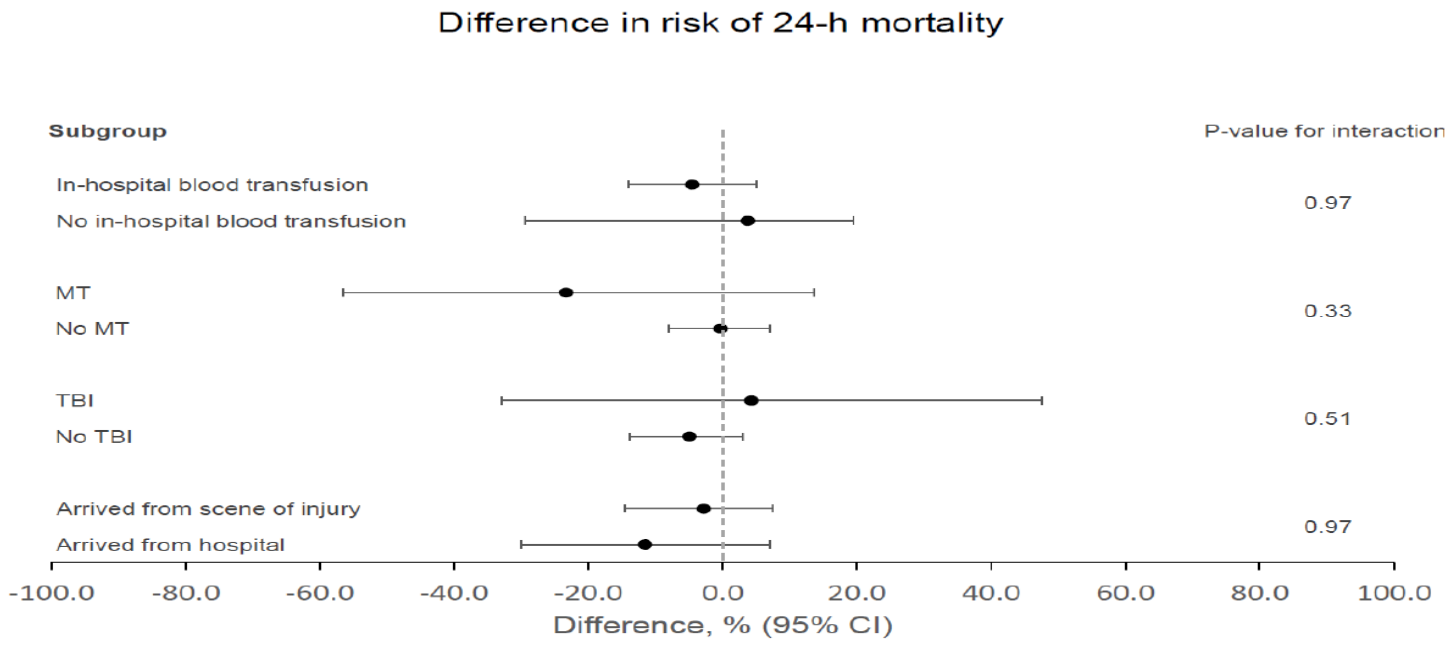
			Unadjusted analysis		Adjusted analysis	
Clinical Outcomes	**Standard Care (N = 98)**	**Cold Stored Platelets (N = 102)**	**Difference (95% CI)**	**p-value**	**OR/ difference (95% CI)**	**p-value**
3-h mortality, No. %	7 (7.1)	6 (5.9)	-1.3% (-9.1, 6.3)	0.72	0.9 (0.3, 2.9)	0.86
In-hospital mortality [c], No. %	13/82 (15.8)	12/91 (13.2)	-2.7% (-13.9, 8.2)	0.62	0.8 (0.3, 1.9)	0.62
30-day mortality [c,d], No. %	13/82 (16)	12/91 (13)	-2.7% (-13.9, 8.2)	0.62	0.8 (0.3, 1.9)	0.62
Mortality from hemorrhage, No. %	7 (7.1)	7 (6.9)	-0.3% (-8.8, 7.4)	0.89	1.0 (0.3, 3.1)	0.99
ARDS, No. %	3/93 (3.2)	6/100 (6.0)	2.8% (-4.0, 9.8)	0.36	2.2 (0.6, 11.0)	0.27
Allergic/transfusion reaction, No. %	0 (0)	0 (0)	-		-	
Thromboembolic events, No. %	10/93 (10.8)	10/100 (10.0)	-0.8% (-10.2, 8.3)	0.86	0.9 (0.4, 2.4)	0.85
Achieve hemostasis, No. %	91/98 (92.9)	95/102 (93.1)	0.3 (-6.8, 7.4)	0.94	1.1 (0.4, 3.2)	0.90
Initial rapid TEG						NS
24-hour rapid TEG						NS
Initial coagulation measurements						NS
24-hour transfusion requirements						NS

CriSP-HS Trial- Prespecified Subgroups

A.

Characteristic	Standard Care n/N (%)	Cold Stored Platelets n/N (%)	Difference in 24-hour mortality
In-hospital blood transfusion			
Yes	10/89 (11.2)	5/75 (6.7)	-4.6
No	0/9 (0.0)	1/27 (3.7)	3.7
Required MT			
Yes	6/15 (40.0)	2/12 (16.7)	-23.3
No	4/83 (4.8)	4/90 (4.4)	-0.4
Severe TBI			
Yes	1/10 (10.0)	1/7 (14.3)	4.3
No	9/88 (10.2)	5/95 (5.3)	-5.0
Arrived from			
Scene of injury	7/64 (10.9)	6/74 (8.1)	-2.8
Referral hospital	3/26 (11.5)	0/19 (0.0)	-11.5

B.



CriSP-HS Trial-Safety

	Standard Care (n = 98)	Cold Stored Platelets (n = 102)
Adverse Events Total	68	61
Serious Adverse Events Total	52	49
Individual Serious Adverse Events with Any Relatedness		
Coagulopathy	0	1
Pneumonia/VAP	1	1
Arterial Thrombosis	1	1
Deep Vein Thrombosis (DVT)	0	2
Pulmonary Embolism (PE)	2	3
Transfusion Associated Cardiac Overload (TACO)	0	1
Serious Adverse Events with Any Relatedness Total	4	9

CriSP-HS Trial-Storage Age CSP

	Cold Stored Platelets Shelf Time			
Clinical Outcome	≤ 7 days (n = 41)	8 – 14 days (n = 57)	Difference (95% CI)	p-value
24-h mortality, No. %	1 (2.4)	2 (3.5)	-1.1% (-10.1,10.1)	0.78
3-h mortality, No. %	1 (2.4)	2 (3.5)	-1.1% (-10.1, 10.1)	0.78
In-hospital mortality, No. %	4/39 (10.3)	5/49 (10.2)	0.1% (-13.5,15.7)	0.99
30-day mortality [b,c], No. %	4/39 (10.3)	5/49 (10.2)	0.1% (-13.5, 15.7)	0.99
Mortality from hemorrhage [b], No. %	3/40 (7.5)	2/56 (3.6)	3.9% (-6.2, 16.9)	0.65
ARDS [b], No. %	3/40 (7.5)	3/56 (5.4)	2.1% (-8.7, 15.6)	0.69
Allergic/transfusion reaction, No. %	0 (0)	0 (0)	-	
Thromboembolic events [b], No. %	4/40 (10.0)	6/56 (10.7)	-0.7% (-0.1, 0.2)	0.91
Initial rapid thromboelastography measurements,[d,e] median (IQR)				NS
24-hour rapid thromboelastography measurements				NS
Initial coagulation measurements				NS
24-hour coagulation measurements				NS
Transfusion requirements within 24-hours				NS

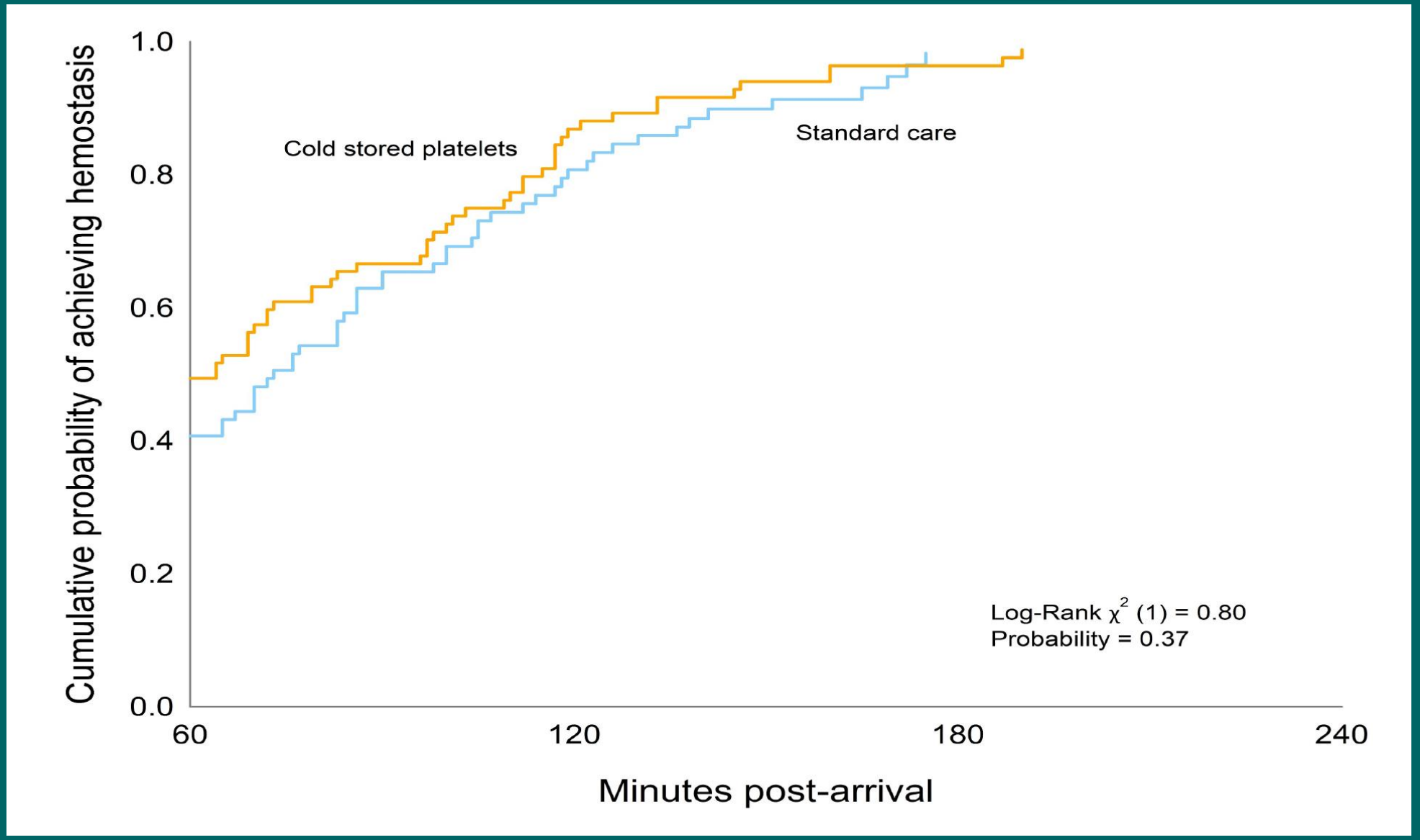
CriSP-HS Trial-Time to platelet transfusion

In those receiving platelets

Median time [IQR] to first platelet
31 [16, 53] mins vs 87 [45, 143] mins, P<0.01

CriSP-HS Trial

Time to Hemostasis



CriSP-HS Limitations

- Phase 2 design; Power
- Lower than expected 24-hr mortality
- Standard Care- Not all received platelets
- Evolving and variability in trauma resuscitation standard care
- Earlier time to platelets for CSP arm

CriSP-HS Summary/Conclusions

- CSP Feasible, Safe for HS
- Lower 24-hr mortality; not significant
- No outcome differences out to 14 days
- Earlier time to platelets for CSP arm

CriSP-HS Trial

RANDOMIZED CONTROLLED TRIAL

OPEN

Early Cold Stored Platelet Transfusion Following Severe Injury

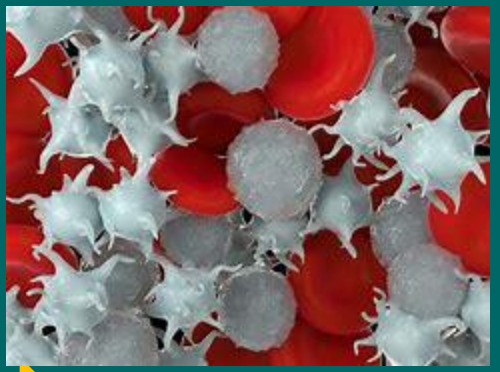
A Randomized Clinical Trial

Jason L. Sperry, MD, MPH,✉ Francis X. Guyette, MD, MPH,†*
Bedda L. Rosario-Rivera, PhD,‡ Matthew E. Kutcher, MD,§
Lucy Z. Kornblith, MD,‖ Bryan A. Cotton, MD,¶
*Chad T. Wilson, MD, MPH,# Kenji Inaba, MD,** Eva V. Zadorozny, PhD,†*
Laura E. Vincent, MS, RN,†† Ashley M. Harner, BS,††
Emily T. Love, BA,†† Joseph E. Doherty, MD, PhD,§ Joseph Cuschieri, MD,‖
Aaron E. Kornblith, MD,‡‡ Erin E. Fox, PhD,¶ Yu Bai, MD, PhD,¶
*Marcus K. Hoffman, MD,# Catherine P. Seger, MD,# Jay Hudgins, MD,***
*Sheila Mallett-Smith, DNP, RN,** Matthew D. Neal, MD,**
Christine M. Leeper, MD, Philip C. Spinella, MD,* Mark H. Yazer, MD,§§*
Stephen R. Wisniewski, PhD,‡ and
the Cold Stored Platelet for Hemorrhagic Shock (CRISP-HS) Study Group

Ann Surg. 2024 Aug 1;280(2):212-221

The Early, Cold? Bird Gets The….

??



TOI

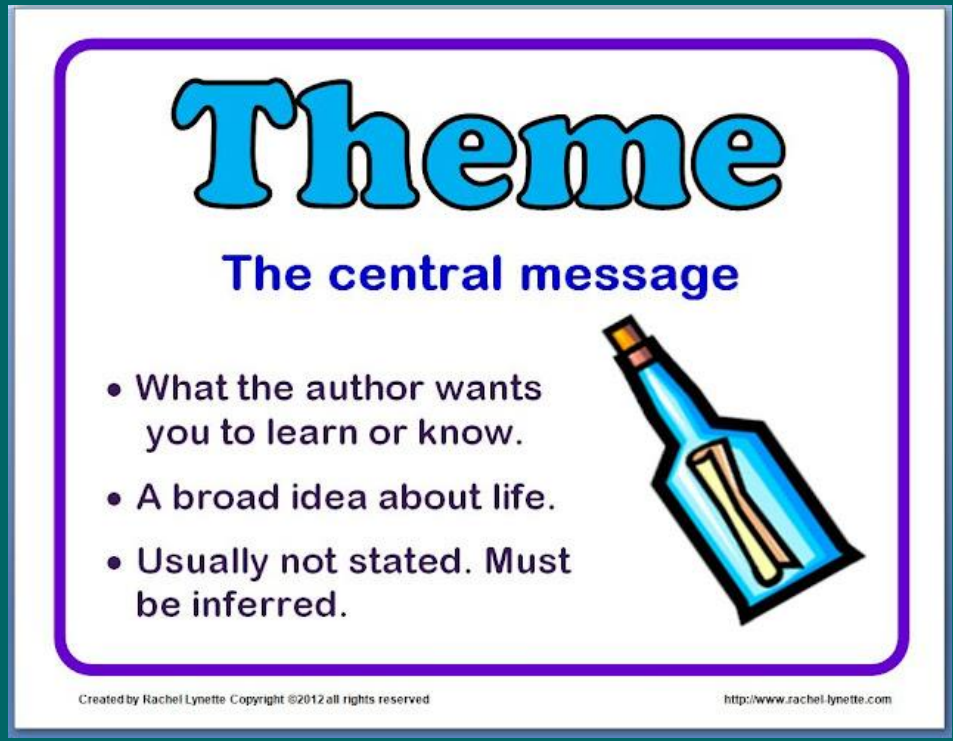
CriSP-TBI Trial

Enrollment Completed-Dr. Neal

- **Time to platelet transfusion**

median time [IQR]

29 [18,61] mins
vs.
130 [72, 218] mins,
P<0.01



CriSP-HS and CriSP-TBI Trials

- **Platelet transfusion- Can be urgently available**

Acknowledgements

- Participating Sites- Site PIs, Research Staff
- LITES / MACRO Research staff- University Pittsburgh
- Data Coordinating Center- University Pittsburgh
- FUNDING - DoD Contract No. W81XWH-16-D-0024, Task Order W81XWH-19-F-0494


LITES