Cold Stored Platelets

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Disclosures

- Consultant
  - Cerus
- Advisory Board
  - CSL Behring, Haima, Octapharma,
- Co-Founder, Chief Medical Officer
  - Kalocyte

Platelet Storage Temp Change

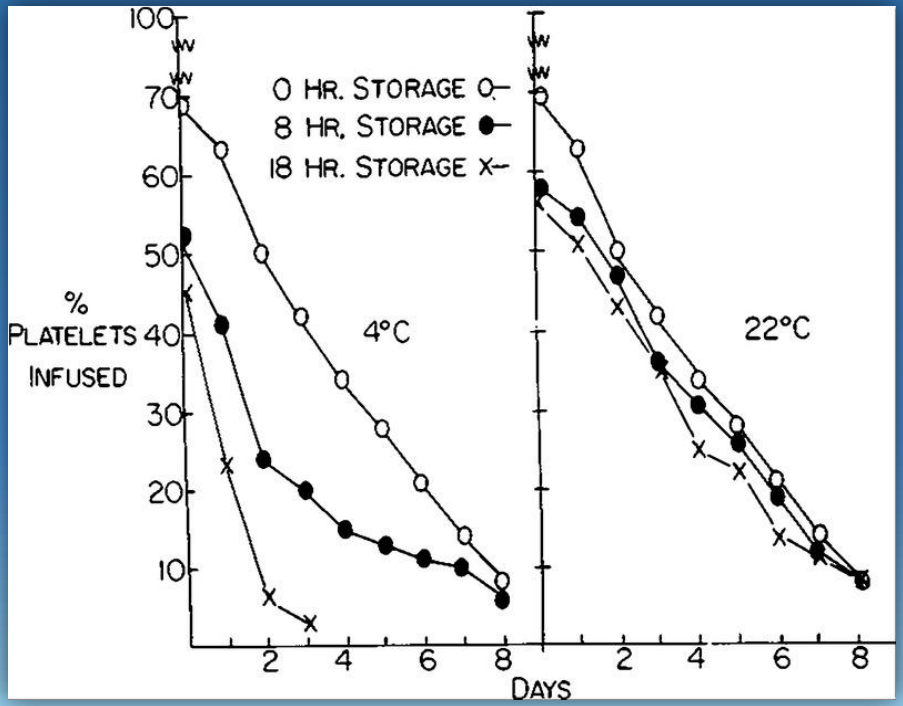
ORIGINAL ARTICLE FREE PREVIEW ARCHIVE

Platelet Preservation — Effect of Storage Temperature on Maintenance of Platelet Viability —Deleterious Effect of Refrigerated Storage

Scott Murphy, M.D., and Frank H. Gardner, M.D.

May 15, 1969
N Engl J Med 1969; 280:1094-1098

"The use of cold platelets should be abandoned...for transfusion purposes"



Cold Storage Increases Hemostasis

TRANSFUSION

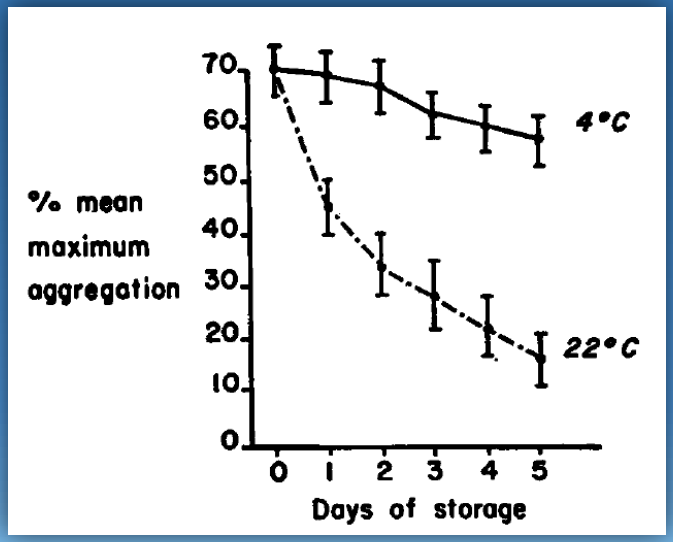
Vol. 13 March-April 1973 No. 2

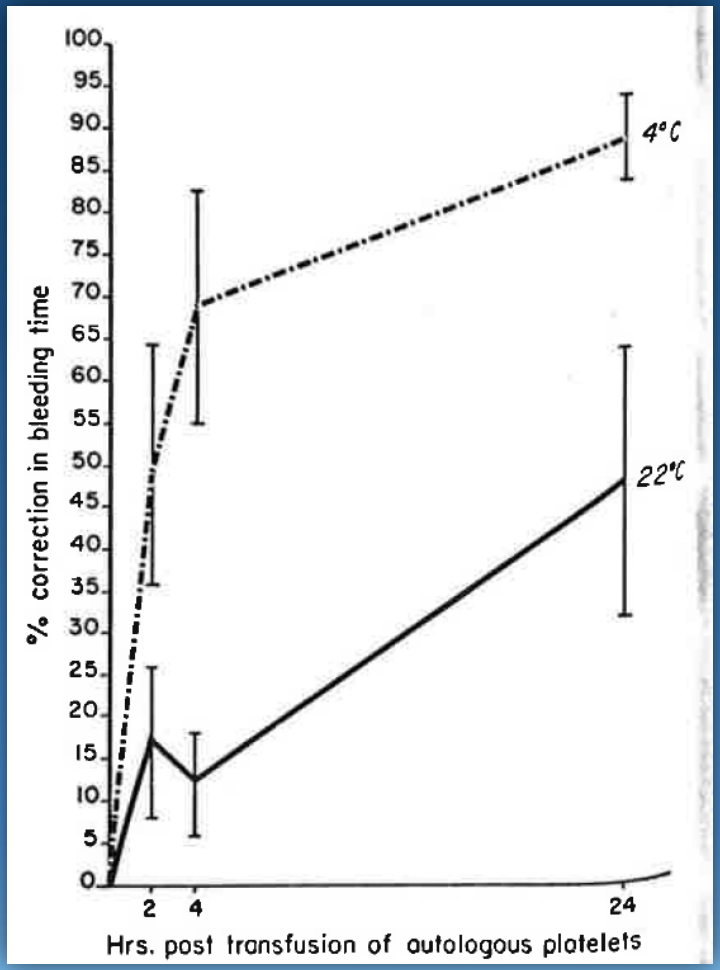
Scientific Articles

Studies of Platelet Concentrates Stored at 22 C and 4 C

G. A. Becker, M. Tuccelli, T. Kunicki, M. K. Chalos and R. H. Aster

Light Transmission Aggregometry





CSP Improved Expected Increase in PLT Count

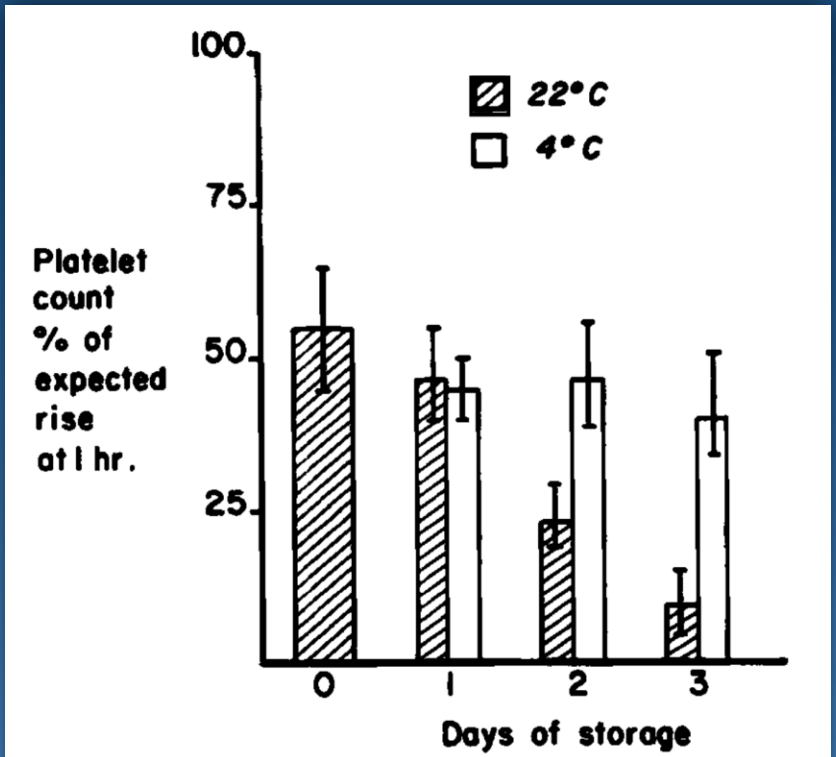


Fig. 4. Platelet increment one hour following transfusion of platelets to thrombocytopenic patients (± 1 standard error of the mean) (S.E.M.). Differences of the means at two and three days are significant ($p < .01$). Calculation of "expected rise" is given in "methods."

Becker. Transfusion. 1973

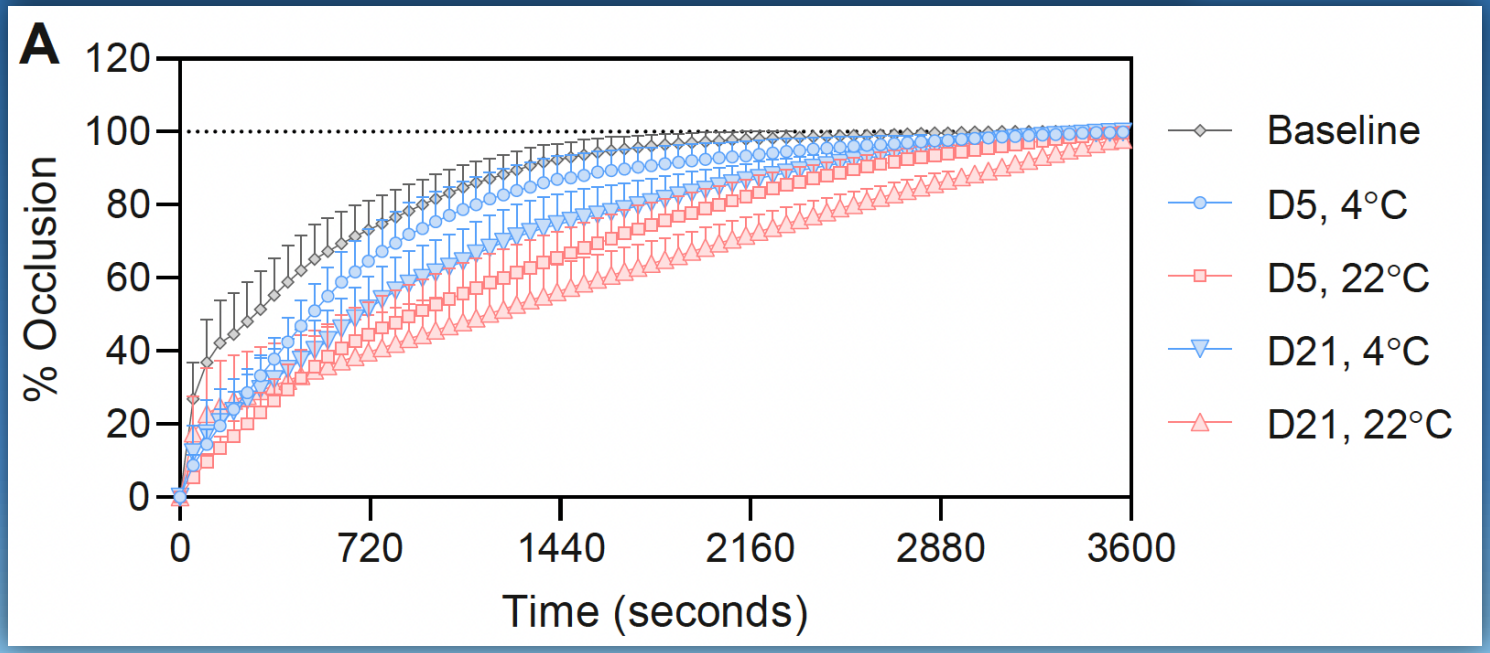
Hemostatic Function of CSP up to 21 days Storage

jth

ORIGINAL ARTICLE

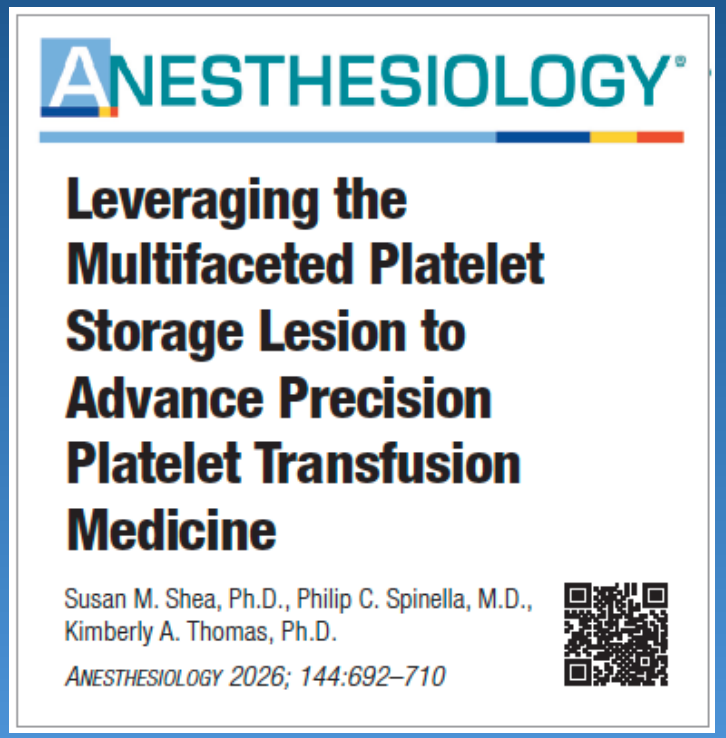
Cold-stored platelet hemostatic capacity is maintained for three weeks of storage and associated with taurine metabolism

Susan M. Shea[1,2] | Julie A. Reisz[3] | Emily P. Mihalko[2] | Katelin C. Rahn[2] | Rassam M. G. Rassam[2] | Alisha Chitrakar[4] | Fabia Gamboni[3] | Angelo D'Alessandro[3] | Philip C. Spinella[1,2,5] | Kimberly A. Thomas[1,4,6]

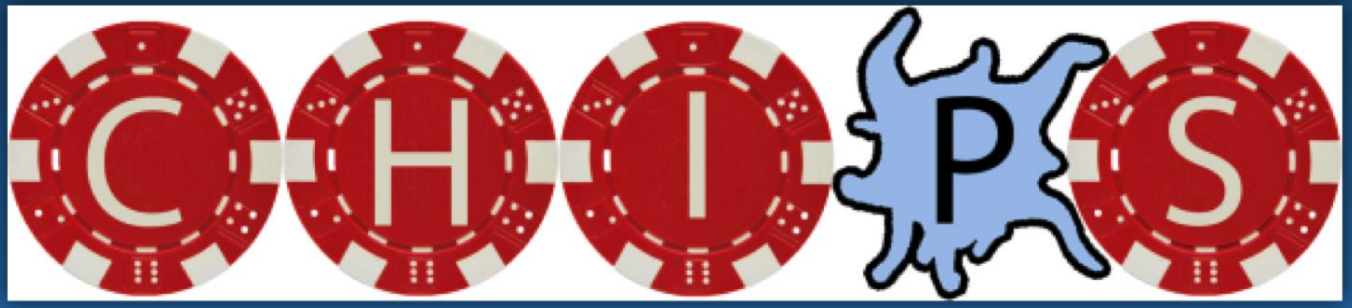


Mechanisms for CSP Improved Hemostasis

- Increased platelet activation
  - P selectin expression
  - Activated GPIIb/IIIa conformation
- Enhanced adhesion to endothelium
  - GP1b-VWF interaction
  - GPVI-collagen interaction
- Increased procoagulant surface
  - Phosphatidylserine externalization
- Greater thrombin generation capacity
- Increased microparticle release
- Preserved mitochondrial function



Shea S, Thomas K, Spinella PC. Blood Transfusion. 2019. 17:321-30



- Chilled Platelet Study
  - Phase 3, international, multi-center, randomized, partially blinded, adaptive, non-inferiority/superiority study
- Co-PI's: Spinella, Steiner, Zantek

CHIPS Design

- Primary endpoint: 5-level bleeding score
- Non-inferiority margin of 1 unit on bleeding score, with gated test for superiority
- Interim analyses every 200 participants
- Maximum sample size of 1000

Interventions

- Room temperature platelets (usual care)
  - Apheresis platform used at the clinical site
- Cold stored platelets
  - Apheresis platforms used at sites
  - Stored 1-6 C
  - Not agitated
  - Placed in cold within 8 hrs
  - No bacterial cultures
- Intervention period: 24 hrs from enrollment
- Randomization: fixed at 2:1 (CSP:RTP)

CHIPS Design

- Storage duration adaptive design to determine the maximum storage for CSP
  - Storage age changed according to prespecified rules
  - Started at 7 days with max of 21 days

Inclusion Criteria

- Greater than 3 kg
- Less than 85 years of age
- Complex cardiac surgery with cardiopulmonary bypass

  Or

  Expectation of requiring platelets for bleeding

Primary Outcome: Peri-Operative Bleeding Score

UDPB SCORE (Bleeding Definition)	Sternal closure delayed	Post-op chest tube blood loss within 12 h (mL)	RBC[a] (units)	Plasma (units)	PLT[b]	Cryo	PCCs	FVIIa	Re-exploration/ tamponade
1 Insignificant	No	< 600	0	0	0	No	No	No	No
2 Mild	No	601–800	1	0	0	No	No	No	No
3 Moderate	No	801–1000	2–4	2–4	Yes	Yes	Yes	No	No
4 Severe	Yes	1001–2000	5–10	5–10	N/A	N/A	N/A	No	Yes
5 Massive	N/A	> 2000	> 10	> 10	N/A	N/A	N/A	Yes	N/A

(a) Patients weighing greater than 50 kg.

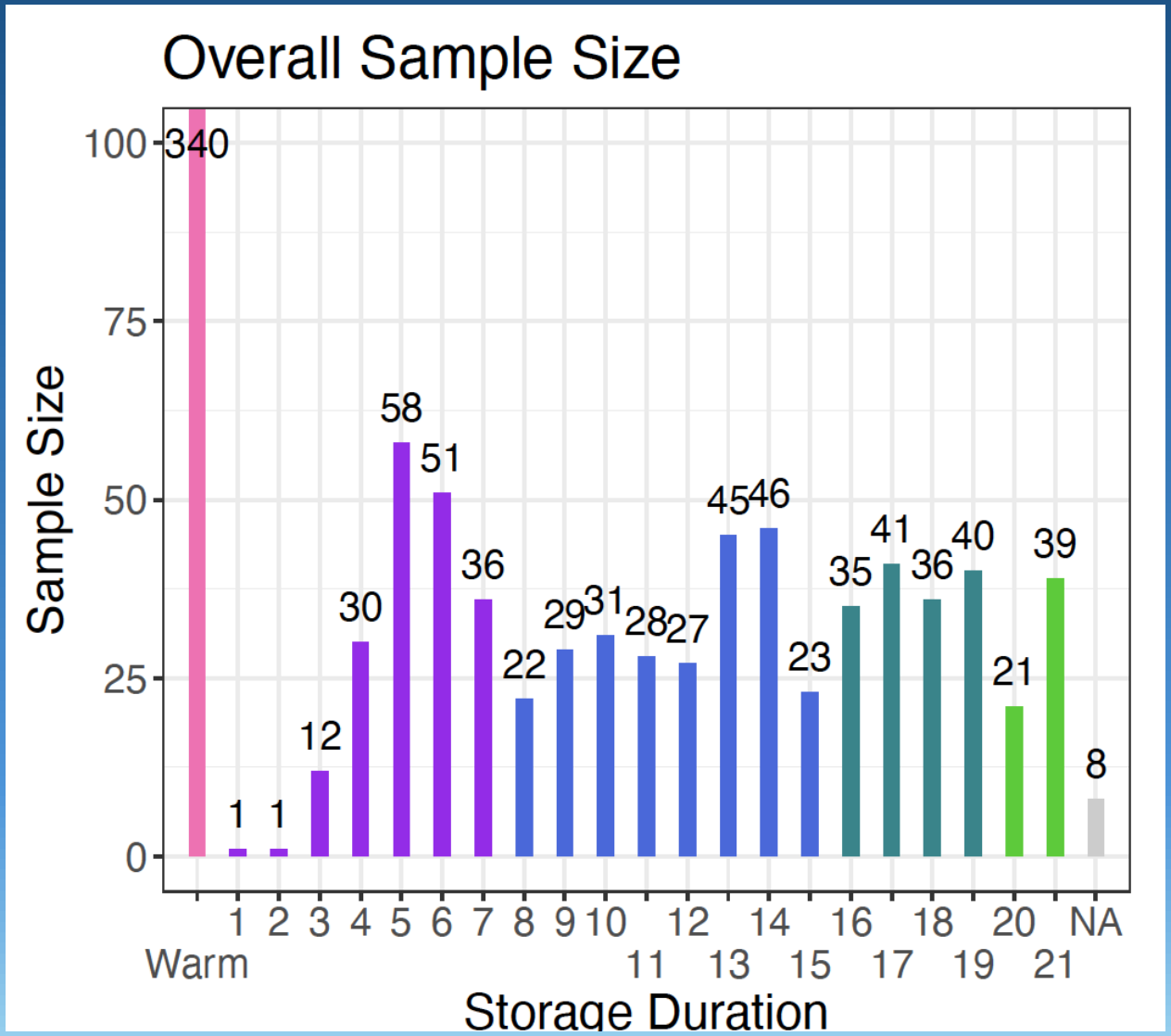
Score calculated after the first platelet transfusion

Dyke C, et al. Universal definition of peri-operative bleeding in adult cardiac surgery. JTCVS 2013.

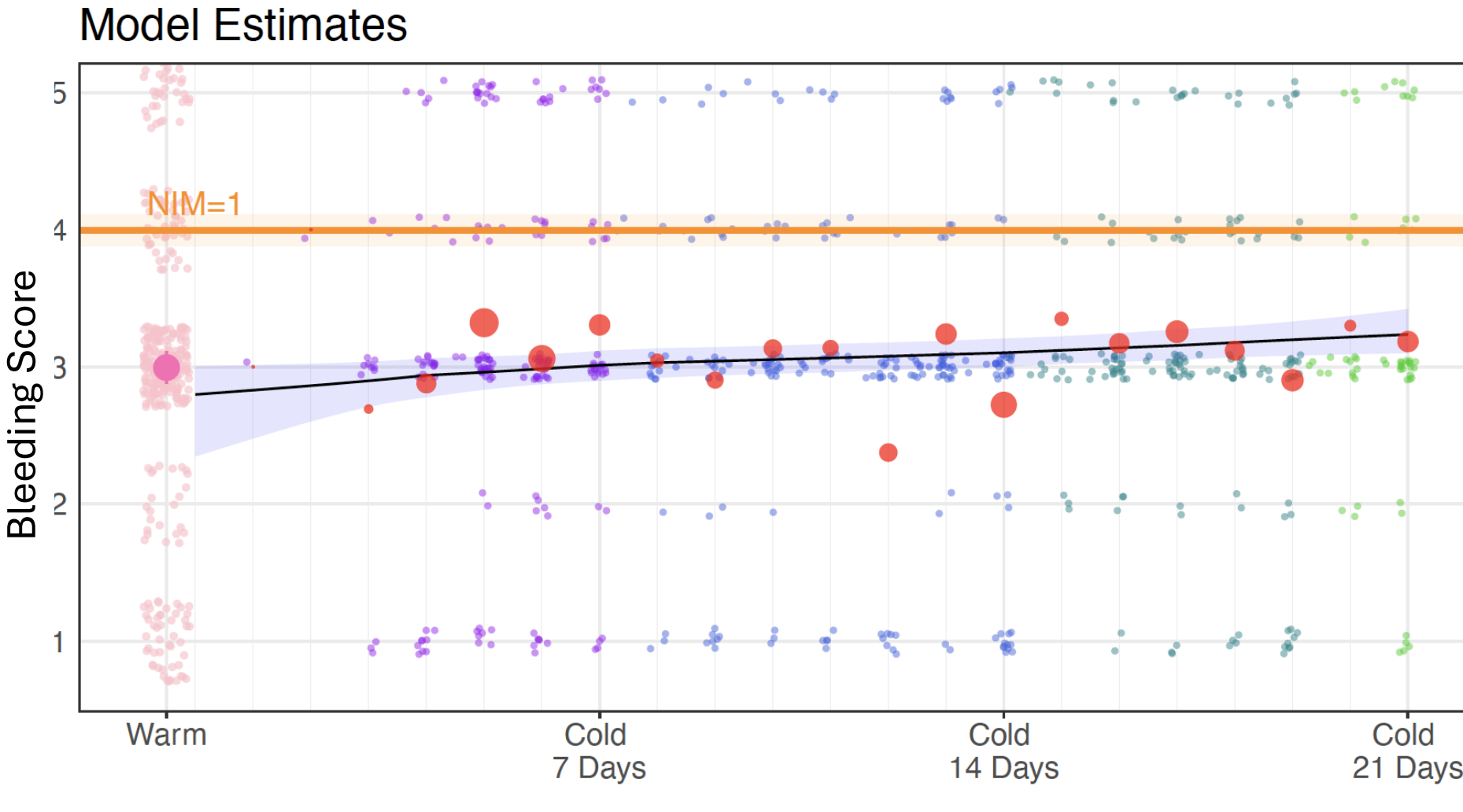
	Overall (N = 1000)	Treatment Assigned: Room temperature (N = 340)	Treatment Assigned: Cold-stored (N = 660)
Age at first study platelet transfusion (years)	42.1 (30.1)	41.8 (30.4)	42.2 (30.0)
Age at first study platelet transfusion (years)			
<12	311 (31.1%)	114 (33.5%)	197 (29.9%)
12-<65	345 (34.5%)	107 (31.5%)	238 (36.1%)
≥65	343 (34.3%)	119 (35.0%)	224 (34.0%)
Sex			
Female	322 (32.2%)	118 (34.7%)	204 (30.9%)
Male	678 (67.8%)	222 (65.3%)	456 (69.1%)
Weight at start of surgery (kg)			
Overall	62.8 (38.5)	60.7 (38.8)	63.9 (38.2)
Participants <12 years at time of platelet transfusion	12.6 (9.1)	12.1 (8.2)	12.9 (9.6)
Participants 12-<65 years at time of platelet transfusion	85.1 (22.8)	85.2 (22.5)	85.0 (22.9)
Participants ≥65 years at time of platelet transfusion	85.9 (20.0)	85.2 (19.7)	86.2 (20.2)
BMI			
Overall	24.7 (7.9)	24.4 (8.0)	24.8 (7.9)
Participants <12 years at time of platelet transfusion	16.0 (2.1)	15.8 (1.8)	16.2 (2.2)
Participants 12-<65 years at time of platelet transfusion	28.5 (6.7)	28.9 (6.6)	28.4 (6.7)
Participants ≥65 years at time of platelet transfusion	28.6 (5.8)	28.6 (5.7)	28.7 (6.0)

	Overall (N = 1000)	Treatment Assigned: Room temperature (N = 340)	Treatment Assigned: Cold-stored (N = 660)
Surgical complexity (participants ≥18 years at time of platelet transfusion)[3]			
1	86/653 (13.2%)	22/222 (9.9%)	64/431 (14.8%)
2	276/653 (42.3%)	99/222 (44.6%)	177/431 (41.1%)
3	181/653 (27.7%)	61/222 (27.5%)	120/431 (27.8%)
4	80/653 (12.3%)	34/222 (15.3%)	46/431 (10.7%)
≥5	30/653 (4.6%)	6/222 (2.7%)	24/431 (5.6%)
STAT Mortality score (participants <18 years at time of platelet transfusion)[2]			
Category 1	82/347 (23.6%)	28/118 (23.7%)	54/229 (23.6%)
Category 2	145/347 (41.8%)	54/118 (45.8%)	91/229 (39.7%)
Category 3	43/347 (12.4%)	13/118 (11.0%)	30/229 (13.1%)
Category 4	72/347 (20.7%)	22/118 (18.6%)	50/229 (21.8%)
Category 5	5/347 (1.4%)	1/118 (0.8%)	4/229 (1.7%)
Total cardiopulmonary bypass duration (hours)	3.0 (1.5)	2.9 (1.4)	3.0 (1.5)
Total aortic cross clamp duration (hours)	1.9 (1.3)	1.8 (1.2)	1.9 (1.4)
Subject received antiplatelet agent			
Preoperative	440 (44.0%)	151 (44.4%)	289 (43.8%)

CSP Age Increased With Adaptive Design Up To 21 days



CSP up to 21 days were non-inferior to RTP



No Difference in Bleeding Score: PRT vs No PRT

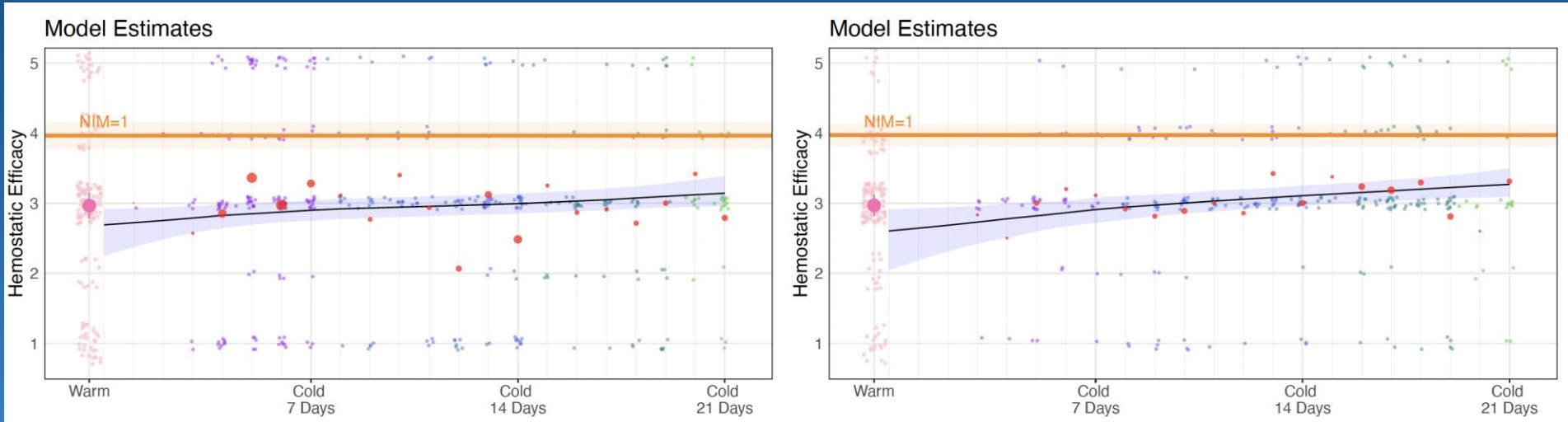


Figure 4.4: Data and model fit individually for subjects with PRT (left panel) or Non-PRT (right panel) status.

24 Hour Chest Tube Output

	Room Temp Platelets	Cold Stored Platelets	P value
24 hr chest tube output (ml/kg)	8.4 (5.5-15.9)	8.9 (5.2-15.4)	0.83

24 Hour Chest Tube Output

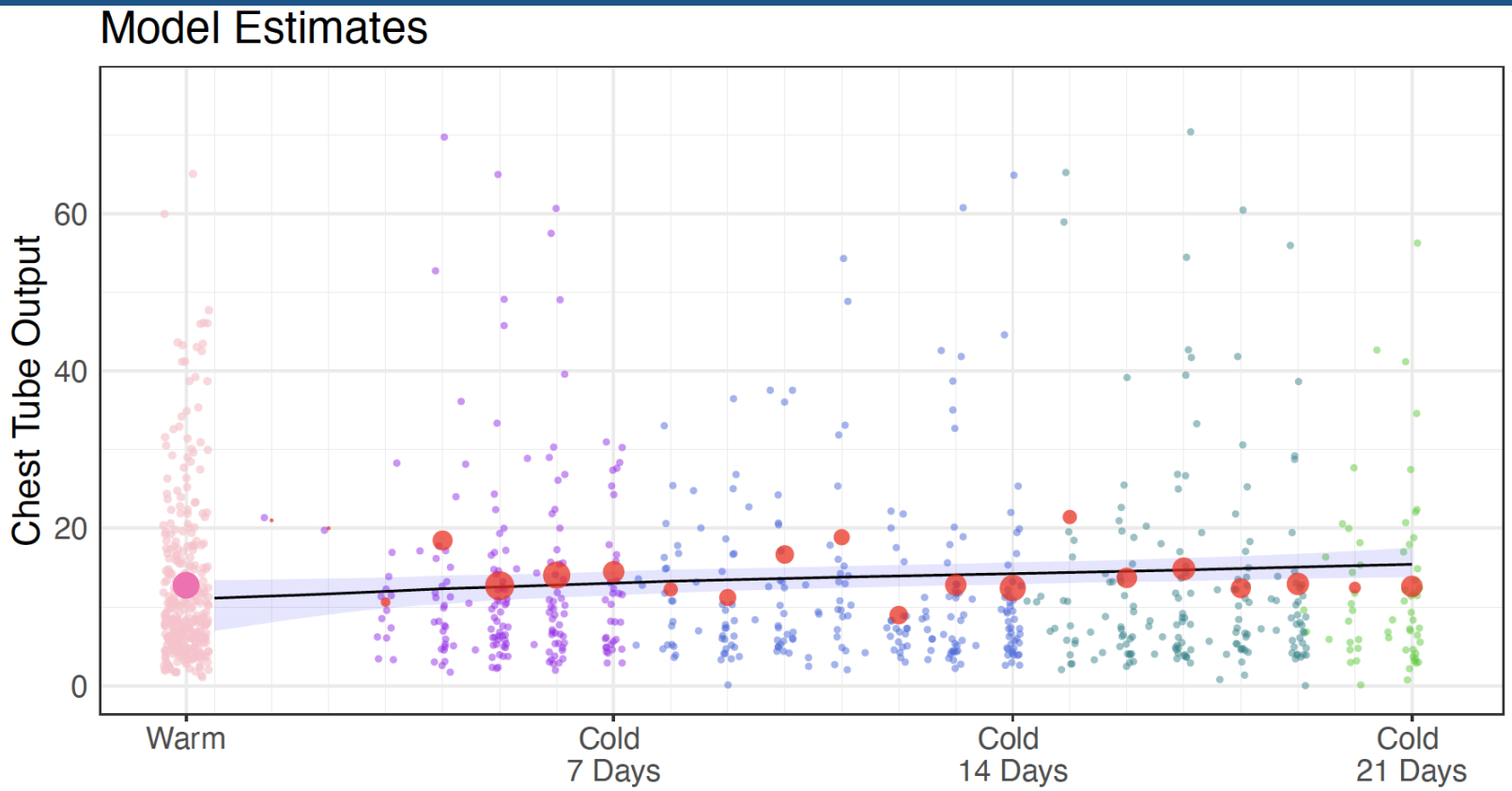


Figure 4.5: Data and model fit for 24-hour chest tube output.

No Difference in Exploratory Outcomes

	Overall (N = 1000)	Treatment Assigned: Room temperature (N = 340)	Treatment Assigned: Cold-stored (N = 660)	Level of evidence
Exploratory Outcomes				
Mechanical ventilation required on or after ICU admission	835 (83.5%)	283 (83.2%)	552 (83.6%)	0.4% (-4.5%, 5.3%)[2]
Ventilator free days	27.0 [27.0, 28.0]	27.0 [27.0, 28.0]	27.0 [27.0, 28.0]	0.0 (-1.0, 1.0)[3]
ICU length of stay (days)[4]	4.0 [2.0, 7.0]	4.0 [2.0, 7.0]	4.0 [2.0, 7.0]	0.0 (-0.5, 0.0)[3]
Hospital length of stay (days)[4]	8.0 [6.0, 14.0]	8.0 [6.0, 13.5]	8.0 [6.0, 14.0]	0.0 (-1.0, 1.0)[3]
Relative change in hemostatic efficacy score from before first platelet transfusion to 24 hours after first platelet transfusion[5]	0.33 [0.00, 2.00]	0.33 [0.00, 2.00]	0.33 [0.00, 2.00]	0.00 (-0.25, 0.33)[3]

No Difference in Thrombotic & Safety Outcomes

	Overall (N = 1000)	Treatment Assigned: Room temperature (N = 340)	Treatment Assigned: Cold-stored (N = 660)	Level of evidence
Transfusion associated adverse event(s) within 7 days of first platelet transfusion	1 (0.1%)	0 (0.0%)	1 (0.2%)	0.2% (-0.1%, 0.4%)[1]
Delayed hemolytic transfusion reaction (DHTR)	1 (0.1%)	0 (0.0%)	1 (0.2%)	0.2% (-0.1%, 0.4%)[1]
Arterial thrombotic event within 7 days of first study platelet transfusion	30 (3.0%)	13 (3.8%)	17 (2.6%)	-1.2% (-3.6%, 1.1%)[1]
Stroke	21 (2.1%)	11 (3.2%)	10 (1.5%)	-1.7% (-3.8%, 0.4%)[1]
Myocardial infarction	3 (0.3%)	0 (0.0%)	3 (0.5%)	0.5% (-0.1%, 1.0%)[1]
Aortic thrombotic event	7 (0.7%)	2 (0.6%)	5 (0.8%)	0.2% (-0.9%, 1.2%)[1]
Other arterial thrombotic event	3 (0.3%)	0 (0.0%)	3 (0.5%)	0.5% (-0.1%, 1.0%)[1]
Venous thrombotic event within 7 days of first study platelet transfusion	23 (2.3%)	6 (1.8%)	17 (2.6%)	0.8% (-1.0%, 2.7%)[1]
Pulmonary embolism	5 (0.5%)	2 (0.6%)	3 (0.5%)	-0.1% (-1.1%, 0.8%)[1]
Deep vein thrombosis	13 (1.3%)	4 (1.2%)	9 (1.4%)	0.2% (-1.3%, 1.6%)[1]
Catheter associated thrombotic event	8 (0.8%)	2 (0.6%)	6 (0.9%)	0.3% (-0.8%, 1.4%)[1]
Mortality within 24 hours of first platelet transfusion	8 (0.8%)	1 (0.3%)	7 (1.1%)	0.8% (-0.2%, 1.7%)[1]
28-day all-cause mortality	27 (2.7%)	6 (1.8%)	21 (3.2%)	1.4% (-0.5%, 3.4%)[1]

No SAEs reported that were related and unexpected

Conclusions

- CSP from 7-21 days have similar function than RTP at 5-7 days.
- CSP can be used for active bleeding for up to 21 days

Conclusions

- CSP appear safe and not associated with thrombotic risks
- Increased availability of platelets for bleeding **major public health benefit**

THANK YOU!

- Investigators at 24 sites
- Clinical Coordinating Center
  - Taegen Sullivan
  - Tina Bockelman
  - Christina Daniel
  - Meghan Huff
- Data Coordinating Center-Utah University
  - John Van Buren
- Medical Monitor
  - Frank Booth
- Berry Consultants and DSMB Chair
  - Roger Lewis
- US Department of Defense/USAMMDA
  - Funding

Questions?


DO THE BEST
YOU CAN UNTIL
YOU KNOW BETTER.
THEN, WHEN
YOU KNOW BETTER,
DO BETTER.
MAYA ANGELOU