



Whole Blood Derived Platelets Stored as a Pool: A Randomized Block Non Inferiority Trial

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Can Platelet Derived from PRP be Stored as a Pool?

Advantages of Pooled Storage

- Facilitates “centralized” TM service (inventory management)
- Standardized pooling process
- Faster availability of product
- Facilitate pathogen inactivation
- Facilitate testing for bacteria
- Potential for 7 day storage

Disadvantages/Concerns of Pooled Storage

- Bacterial contamination
- Leukocyte interactions



Every good idea has already been thought of!



*Snyder et al (Transfusion 29:390, 1989)
Moroff et al (Transfusion 33:374, 1993)

- in vitro tests
- “in vivo” assessment* (1 hr CCI and reactions)
- mixed lymphocyte reactions*
 - monoclonal Ab activated T cells
 - ³H-thymidine uptake
- bacterial contamination

Conclusion: Pooled platelet storage is acceptable



POPS 1 and POPS 2

POoled Platelet Storage

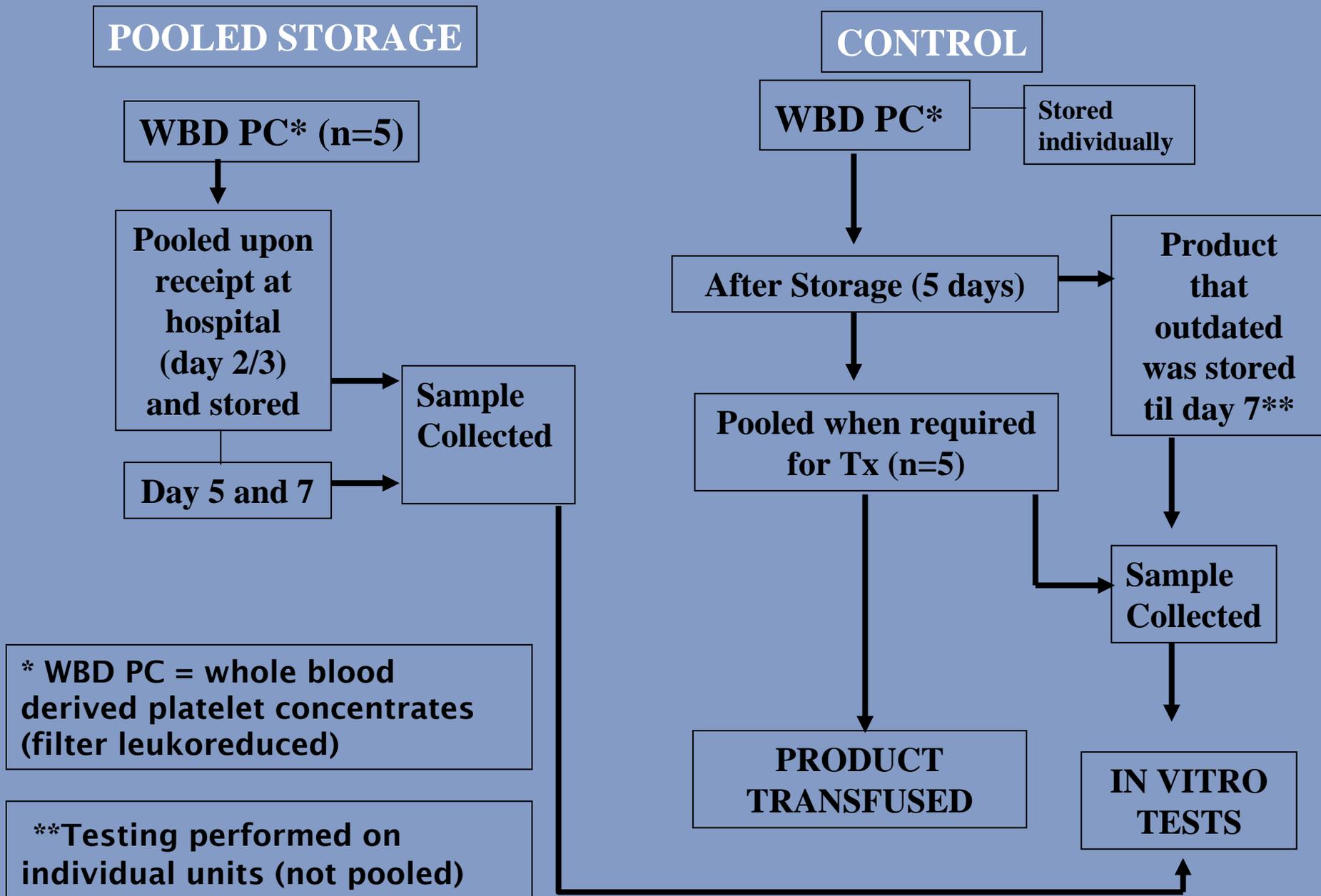


Study

Phase I: To compare “in vitro” properties of filter leukoreduced whole blood derived platelets stored as a pool for 5 and 7 days to platelets stored individually. (POPS 1)

Phase II: To compare the “*in vivo*” effectiveness of platelets stored as a pool to those stored individually for 5 days, by assessing 18 -24 hour CCI and the frequency of adverse events/bleeding. (POPS 2)

POPS 1 Study Design





In vitro Tests

Compliance with Minimum Requirements

- platelet & leukocyte count
- swirling
- pH

Metabolic Activity

- pO_2 and pCO_2
- Lactate production

Shape Change/Morphology

- Morphology score
- Osmotic reversal reaction (HSR)
- Extent of shape change (ESC)

Platelet Activation (secretion/lysis)

- P-selectin
- LDH (supernatant)

Bacterial culture

Leukocyte Activation (flow cytometry CD 69)



Summary of Test Results (POPS 1)

Pooled Storage vs Individual Platelet Storage

Test	Significantly Different		Within Acceptable Range Both Days
	Day 5 (n = 31 to 38)	Day 7 (n = 25 to 30)	
Platelet Count	No	No	Yes
pH	Yes	Yes	Yes
pO ₂	Yes	Yes	Yes
pCO ₂	No	Yes	Yes
Lactate	Yes	Yes	Yes
LDH	Yes	Yes	Yes
Morphology Score	No	Yes	Yes
ESC	No	No	Yes
HSR	No	Yes	Yes
Swirl	No	No	Yes
P Selectin	No	No	Yes



Bacterial Culture

One positive culture:

- control platelets (5 days)
- coagulase negative staphylococcus
- “skin contaminant”



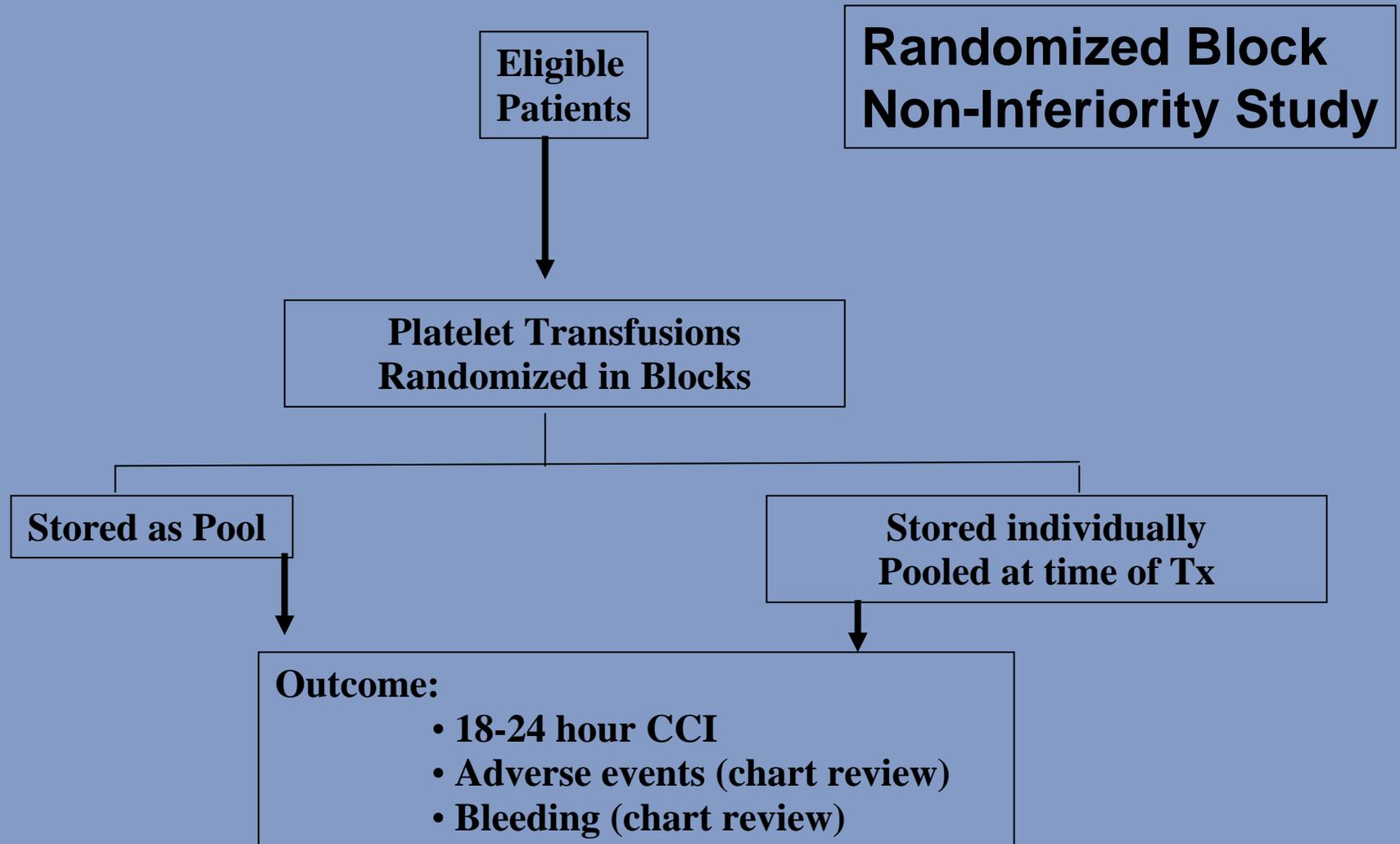
POPS 2: Objective

To determine if the 18 to 24 hour corrected count increments (CCI) of whole blood derived platelets stored as a pool is **not inferior** to the CCI of platelets stored by the routine method (individual unit storage).

Randomized block non-inferiority design

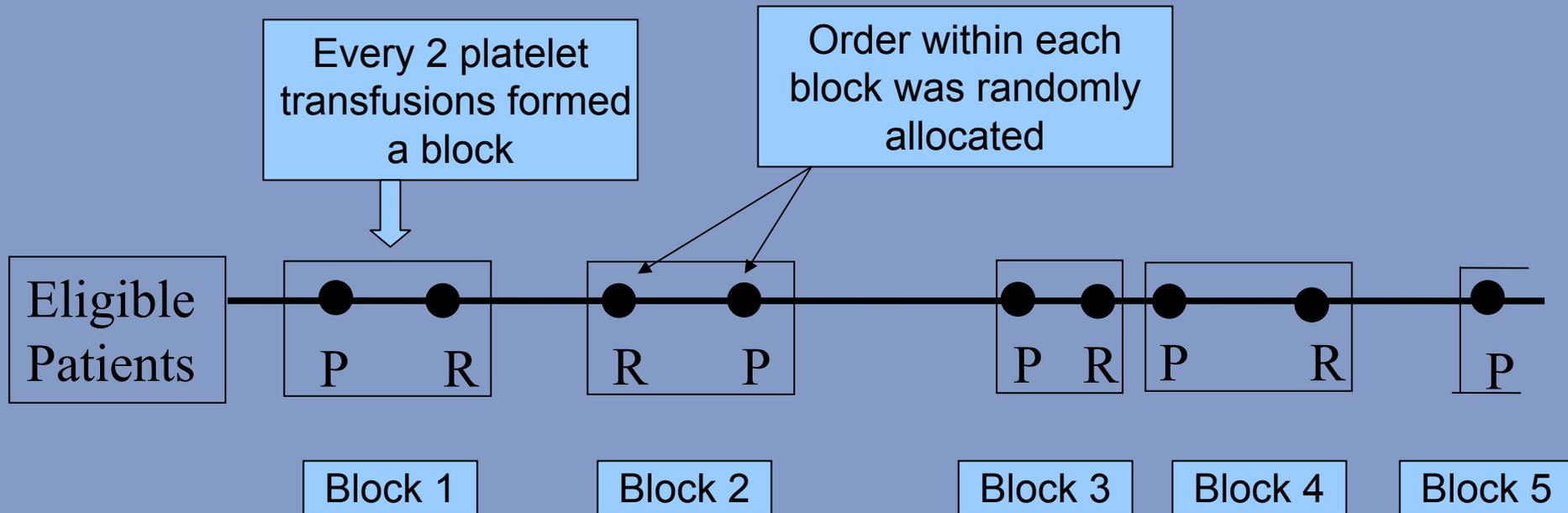


Summary of the POPS 2 Study Design





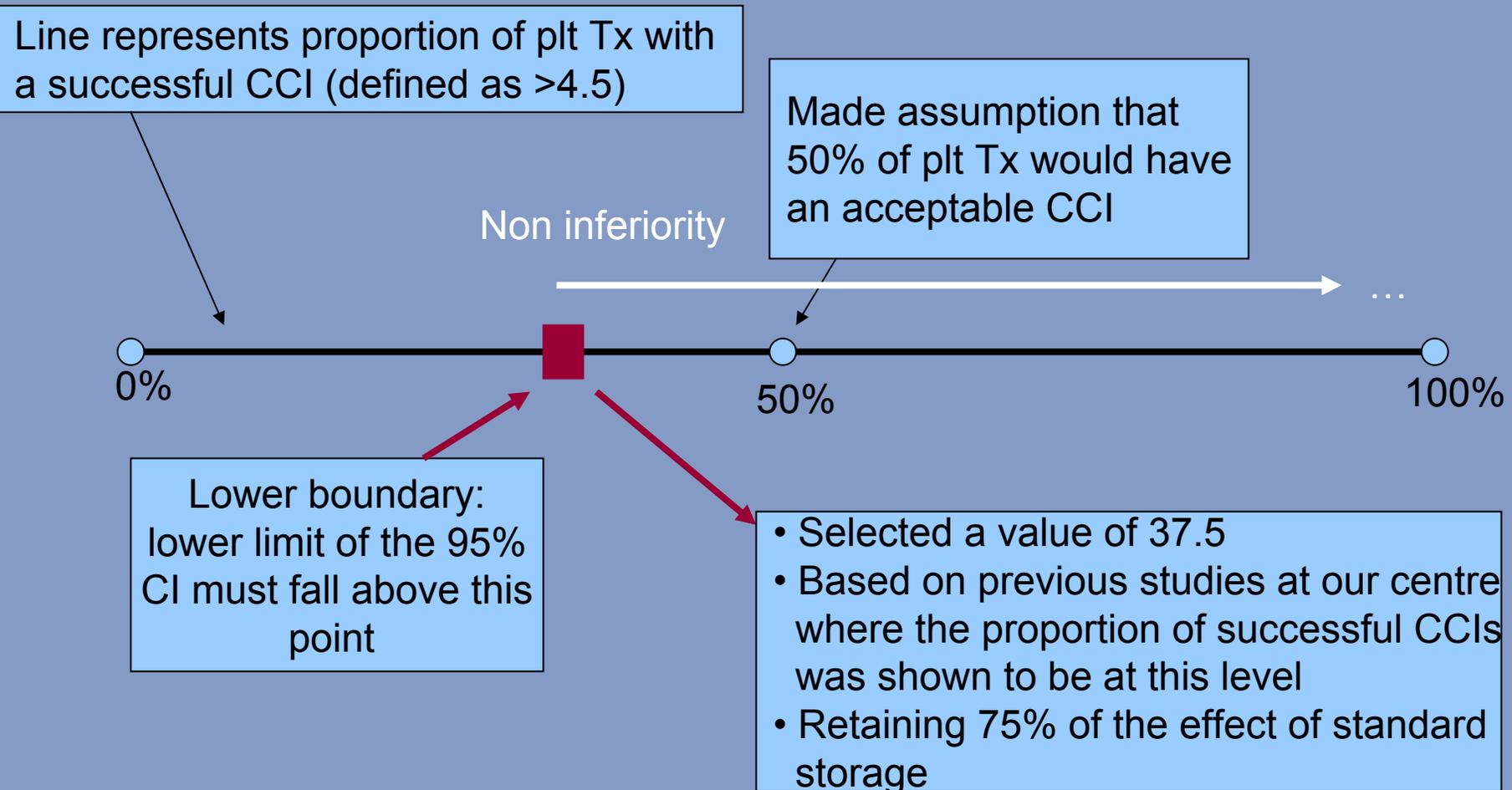
Randomized Block Design



P = Pre-storage Pooled Platelets
R = Routine storage (individual units)



Non-Inferiority Study



Hypothesis

Ho: $RR \leq 0.75$ vs HA: $RR > 0.75$



Eligibility Criteria

Inclusion Criteria

- Hematology/oncology pts
- Multiple platelet transfusions

Exclusion Criteria

- Pts requiring apheresis plts

Temporary Exclusions

- Bleeding (hemodynamically unstable)
- Clinical evidence of DIC (temporarily)
- Out-patients,



Intervention

Standard platelet storage*

- WBD platelets (PRP)
- Stored 22°C with agitation
- Pooled when requested for transfusion(5/pool)

Pre-storage pooled platelets*

- Pooled (n = 5) when received from the blood centre (usually day 2)
- 1000 ml storage bag (CLX plastic)
- Stored as a pool 22°C with agitation

When issued for transfusion:

- Sample collected for platelet count
- Bag weighed

* Screened for bacterial contamination (BacT-Alert-3D)



Outcome Measure

Primary: 18-24 hour CCI

- Successful CCI >4.5
- Reflects clinical practice
- 1 hr and 20 hr CCI are highly correlated*
 - * Bishop et al, TRANSFUSION 1991
- 1 hour CCI may increase the risk of infection (increased access to Hickman catheter)

Secondary Outcomes

- Adverse events and bleeding (chart review)



Patient Demographics (N = 23*)

Demographics	Number	%
Diagnosis		
AML	17	73.9
Lymphoma	2	8.7
ALL	3	13.0
Myelodysplastic Syndrome	1	4.3
Gender		
Male	10	43.5
Female	13	56.5
Previous Transfusions		
YES	21	91.3
NO	2	8.7

*Median age: 53 years (min 19; max 78)



Platelet Product Characteristics

Product Characteristics	Standard Plt Storage (n = 86)	Pre-storage Pooled Platelets (n =86)
Mean absolute plt count x 10 ⁹ /product (SD)	350 (79)	347 (70)
Median product age (days)	4	4
Q1	3	3
Q3	5	5
Minimum	2	2
Maximum	5	5
ABO Compatibility # (%)		
ABO identical	61 (70.9)	61 (70.9)
Major incompatibility	13 (15.1)	15 (17.4)
Minor incompatibility	12 (14.0)	10 (11.6)
# products +ve for bacteria	0	0



Results

- 23 patients
- 189 platelet transfusions
 - 85 complete blocks (17 incomplete blocks; 1 block missing CCI)

POOLED STORAGE

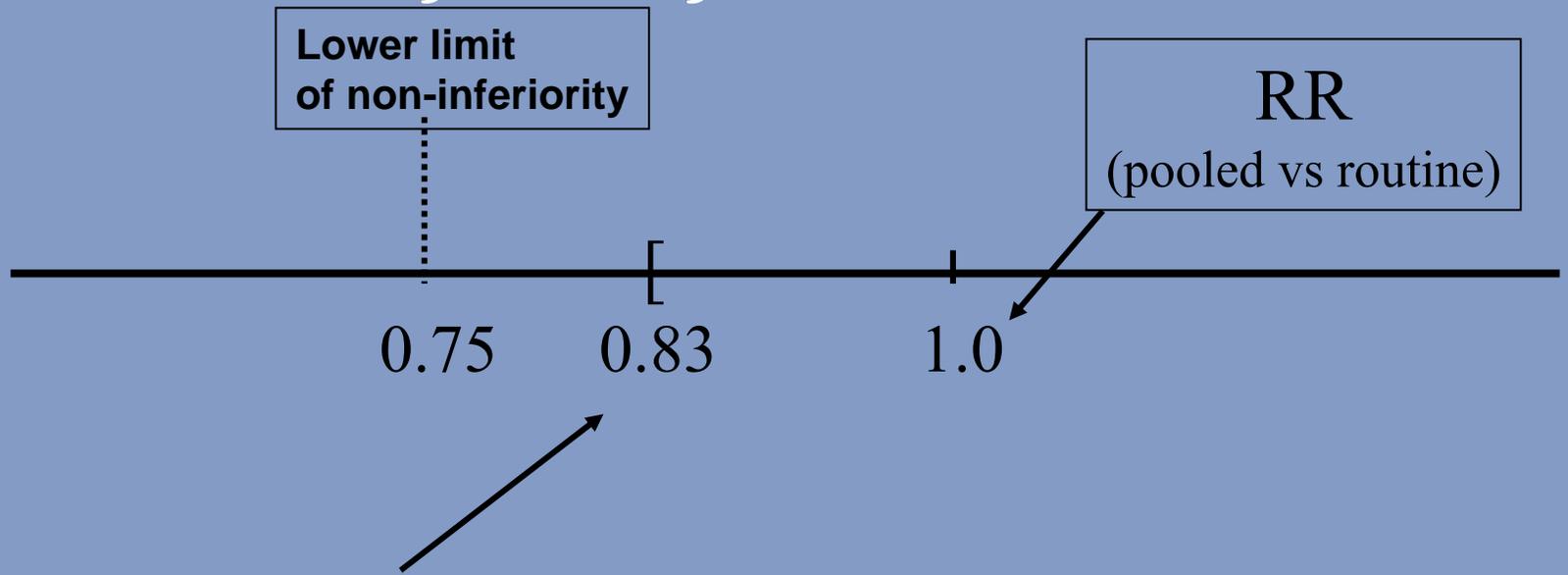
		CCI>4.5	CCI≤4.5	Total
ROUTINE STORAGE	CCI>4.5	32	13	45
	CCI≤4.5	13	27	40
Total		45	40	85

Pooled storage success rate 45/85 (52.9 %)

Routine storage success rate 45/85 (52.9 %)



Non Inferiority Analysis



A lower one-sided 95% CI for the RR was:

$[0.83, \infty]$

Assuming independence between pairs within subjects

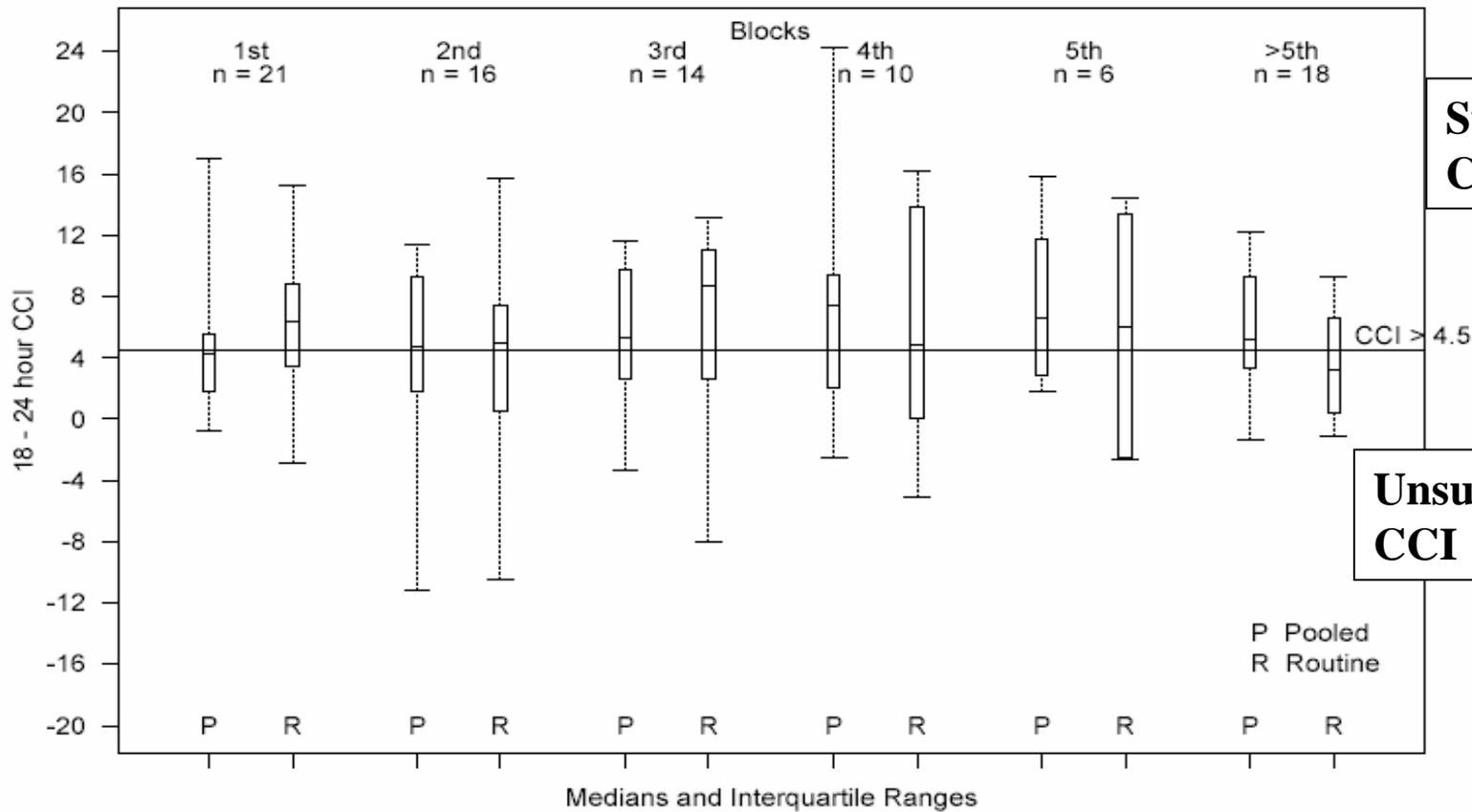
$[0.85, \infty]$

Accommodating association between pairs within subjects

Test of non-inferiority (Tang et al., $p = 0.008$)

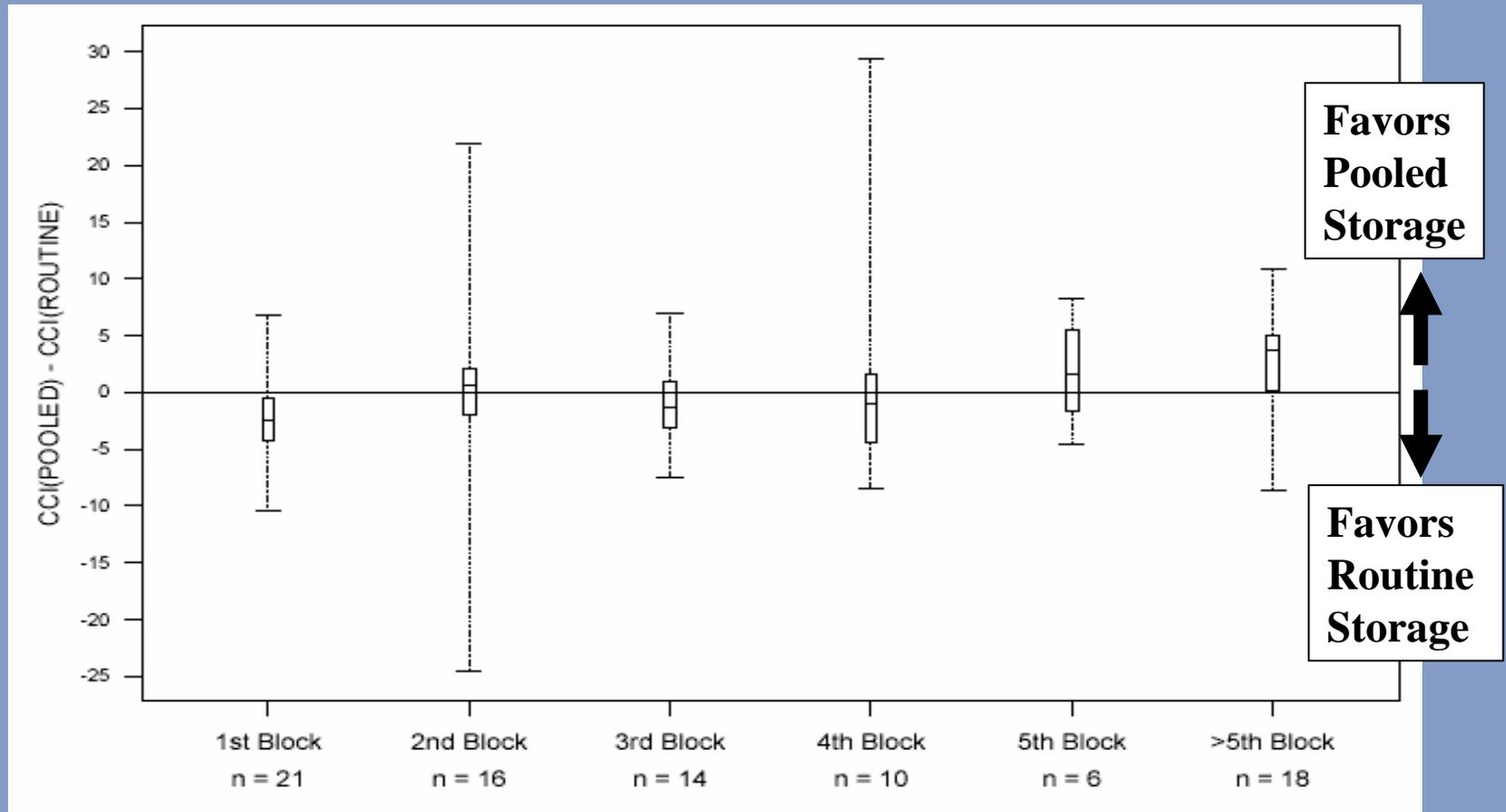


Median CCIs by Product Type by Block





Difference in CCI by Block Based on Complete Blocks





Analysis Treating CCI as a Continuous Variable

	Mean CCI
Pooled storage	5.25
Routine Storage	5.32
Difference	-0.07
95% CI	(-1.47, 1.35)

A random effects model is required to estimate the effect on CCI to account for the lack of independence in responses within subjects over successive transfusions i.e. random effects model gives -0.45 95% CI (-2.23, 1.33)



Adverse Events n = 189

	Pooled Storage	Routine Storage	Total
No Reaction	84	92	176
Reaction	9	4	13
	93 (9.7%)	96 (4.2%)	189

P = 0.16 (Fisher's Exact)



Adverse Events

6.9% of transfusions (13/189) were associated with reactions

9 patients had 13 reactions

- 5 reacted to pre-storage pooled only
- 1 reacted to routine only
- 3 reacted to both

Reaction Type	Pre-storage Pooled Platelets	Routinely Stored Platelets
Febrile Rx	6	1
SOB	1	1
Allergic	1	2
Febrile + Allergic	1	0
TOTAL	9	4



Bleeding Days n = 189

	Pooled Storage	Routine Storage	Total
No Reaction	83	91	174
Reaction	10	5	15
	93 (10.6%)	96 (5.2%)	189

P = 0.10 (Fisher's Exact)



Bleeding Events

9 patients had 15 days with a bleeding event

Type of bleeding	Pre-storage pooled platelets	Routinely stored platelets
Petechiae	3	1
Mucocutaneous	2	2
Echymosis	1	0
Mucocutaneous + Echymosis	1	0
Purpura	3	0
Conjunctival	0	2
TOTAL	10	5

All events were WHO grade 1 bleeding

ACBSA



Conclusion POPS 2

- The 18 to 24 hour CCI for pre-storage pooled platelets was not inferior to that of platelets stored as individual units (RR = 1)
- The frequency of adverse event was not significantly different with the two types of storage and all reactions noted were mild.
- All bleeding episodes noted in the two groups were mild (WHO Grade 1) and the frequency of bleeding days between the two groups was not statistically significant.



Conclusions POPS 2

- This study provides strong evidence that whole blood derived platelets can be stored as a pool for up to five days.



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