Leukoreduction has its place. Is it with LTOWB for *bleeding patients*?

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Disclosures

- Grífols: Honoraria & SAB
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- Verax Biomedical: Scientific advisory board
- Hemanext: Scientific advisory board
- Legacy Innovations: Consultant
- Velico: Equity

Jaffo Gate, Jerusalem

YAZER DESIGN STUDIO

COMMENTARY
Transfusion Practice

THOR-AABB JOINT WORKING GROUP

TRANSFUSION

It is time to reconsider leukoreduction of whole blood for use in patients with life-threatening hemorrhage

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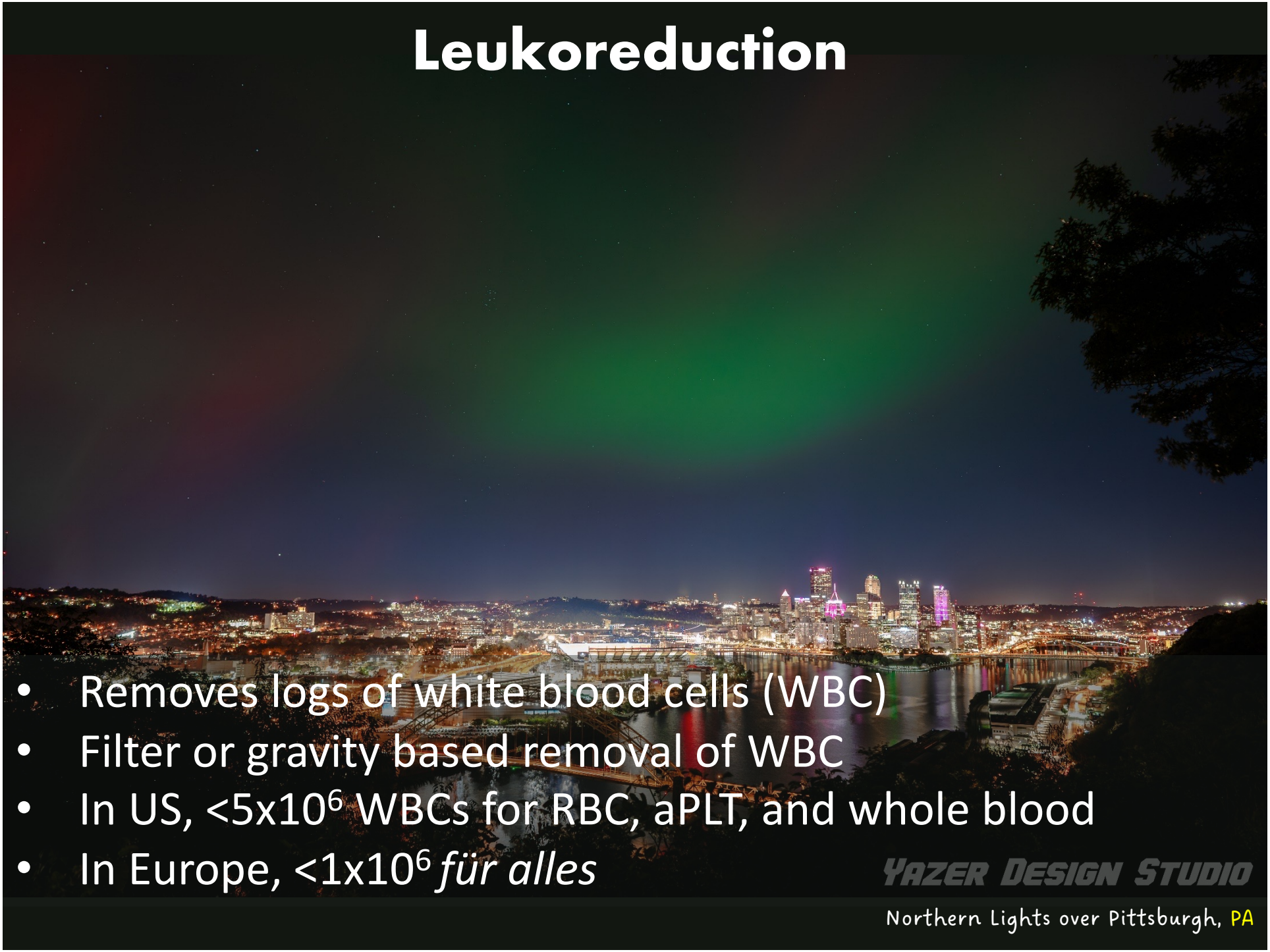
Leukoreduction

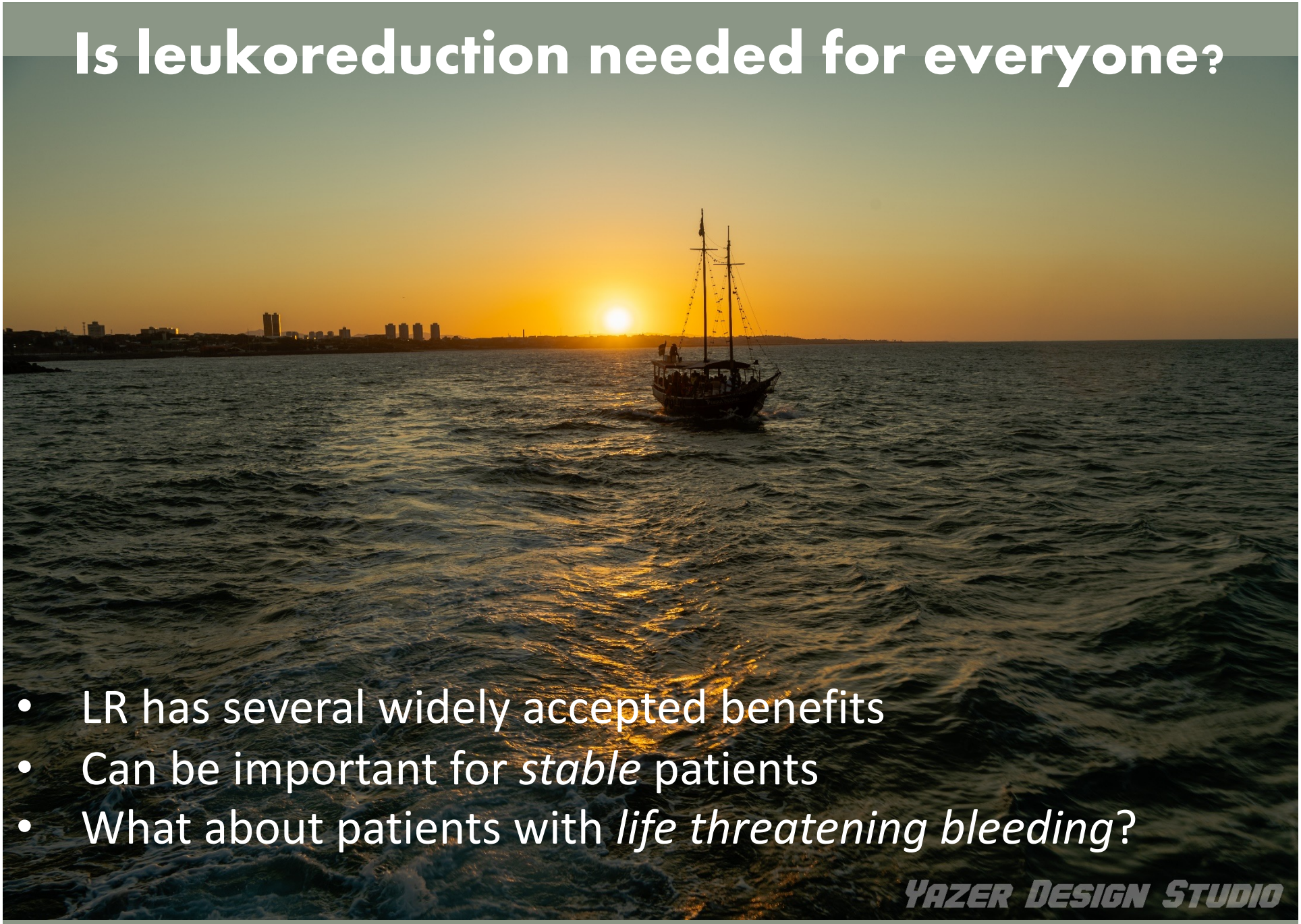


- Removes logs of white blood cells (WBC)
- Filter or gravity based removal of WBC
- In US, <5x10^6 WBCs for RBC, aPLT, and whole blood
- In Europe, <1x10^6 *für alles*

YAZER DESIGN STUDIO

Northern Lights over Pittsburgh, PA

Is leukoreduction needed for everyone?



- LR has several widely accepted benefits
- Can be important for *stable* patients
- What about patients with *life threatening bleeding*?

Fortaleza, Brazil

Several accepted benefits of LR: 1

- Reduces febrile reactions

Reduces febrile reactions

- Prestorage LR removes an important source of cytokines before they can be released into the product
- Can be very uncomfortable for patients but not life threatening

	PrUR RBC	PoUR RBC	PrUR PLT	PoUR PLT
Dates	July 1997-July 1999	August 1999-August 2001	July 1997-January 1998	February 1998-August 2001
RBCs transfused (number)	70,396	72,949	NA	NA
PCs transfused (number)	n/a	n/a	6502	50,555
Total adverse reactions (number)	486	398	165	695
FNHTRs (RBC or PC)	231	136	29	56
Rate FNHTR (RBC or PC, percent)	0.33	0.19*	0.45	0.11*
Transfusion reactions (percent)	48	34*	18	8*

* $p < 0.001$.

Yazer MH et al. *Transfusion* 2004;44:10-15

Thanks for the photo, Phil

Several accepted benefits of LR:2

- Reduces CMV and HTLV transmission

Reduces CMV transmission

- 502 bone marrow transplant recipients were randomized to receive CMV seronegative or LR blood products
- LR was equivalent to using seronegative donors in the primary analysis

CMV Event	Seronegative Blood (N = 252)	LR (N = 250)	*P* Value*
Primary analysis (day 21-100)			
All CMV infections + disease	2 (1.3%)	3 (2.4%)	1.0
CMV disease only	0 (0%)	3 (1.2%)	0.25
Secondary analysis (day 0-100)			
All CMV infections + disease	4 (1.4%)	6 (2.4%)	0.5
CMV disease only	0 (0%)	6 (2.4%)	0.03
Survival	79%	82%	0.56

Bowden RA et al. *Blood* 1995;86:3598-3603

Thanks for the photo, Beckett

Several accepted benefits of LR:3

- Reduces HLA alloimmunization

Reduces HLA alloimmunization

- 603 patients with acute myeloid leukemia
- Significantly lower immune PLT refractoriness amongst those who received filter/apheresis LR PLTs vs. control

100

Control Unmodified pooled PLT

TABLE 2. Linear probability model for HLA antibody prevalence*

Donor group	Additive risk (%) for HLA alloimmunization (95% CI)	p value
Deliveries†		
Zero deliveries	0.0	<0.0001
One delivery	14.5 (11.7-17.3)	
Two deliveries	21.9 (19.7-24.0)	
Three deliveries	29.0 (25.9-32.0)	
Four or more deliveries	32.4 (28.0-36.8)	
Lost pregnancies‡		
Zero lost pregnancies	0.0	0.02
One lost pregnancy	–0.4 (–1.7-0.9)	
Two or more lost pregnancies	4.5 (1.3-7.7)	

Weeks

Kakaiya RMTRAP Trial. TransNEJM 1997;337:1828-1869

Thanks for the photo, Phil

Some possible benefits of LR

- Might reduce/eliminate transfusion related immunomodulation (TRIM)
- Might prevent transfusion associated graft vs host disease (TA-GVHD)

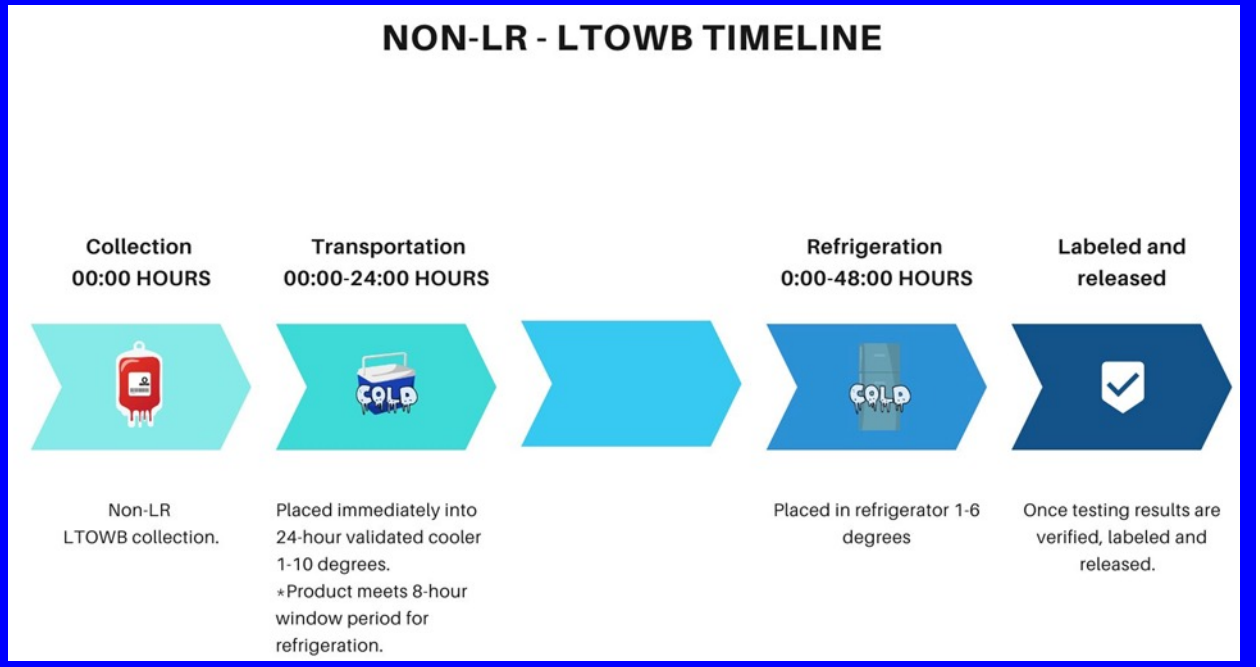
Jerusalem, Israel

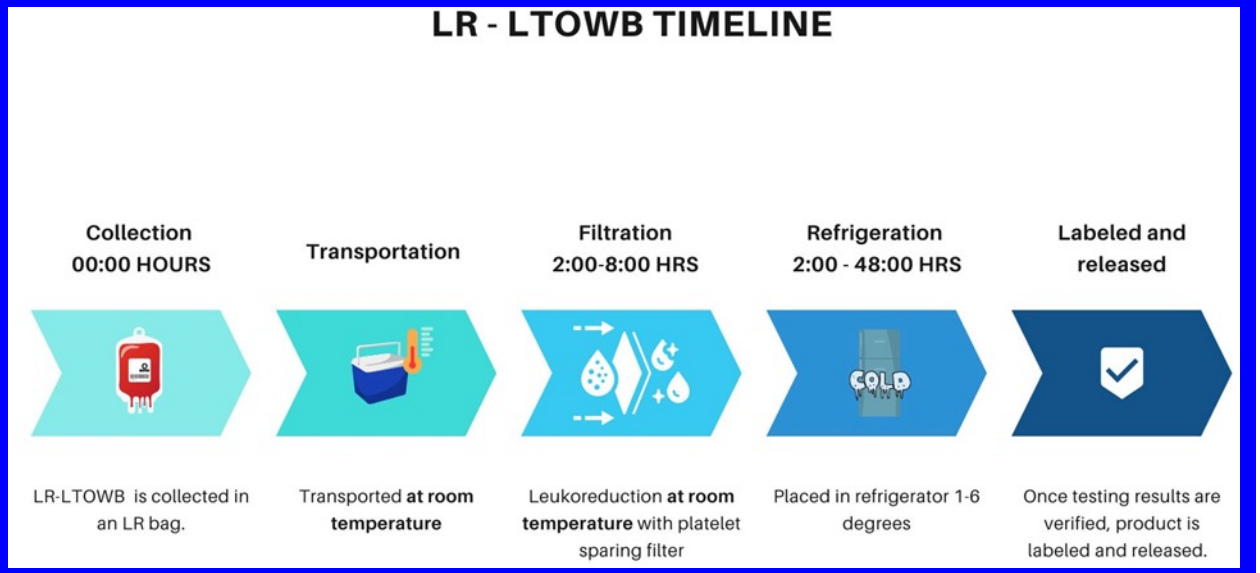
Thanks for the photo, Beckett

Several problems with WB LR:1

Must be filtered within 8 hours of collection

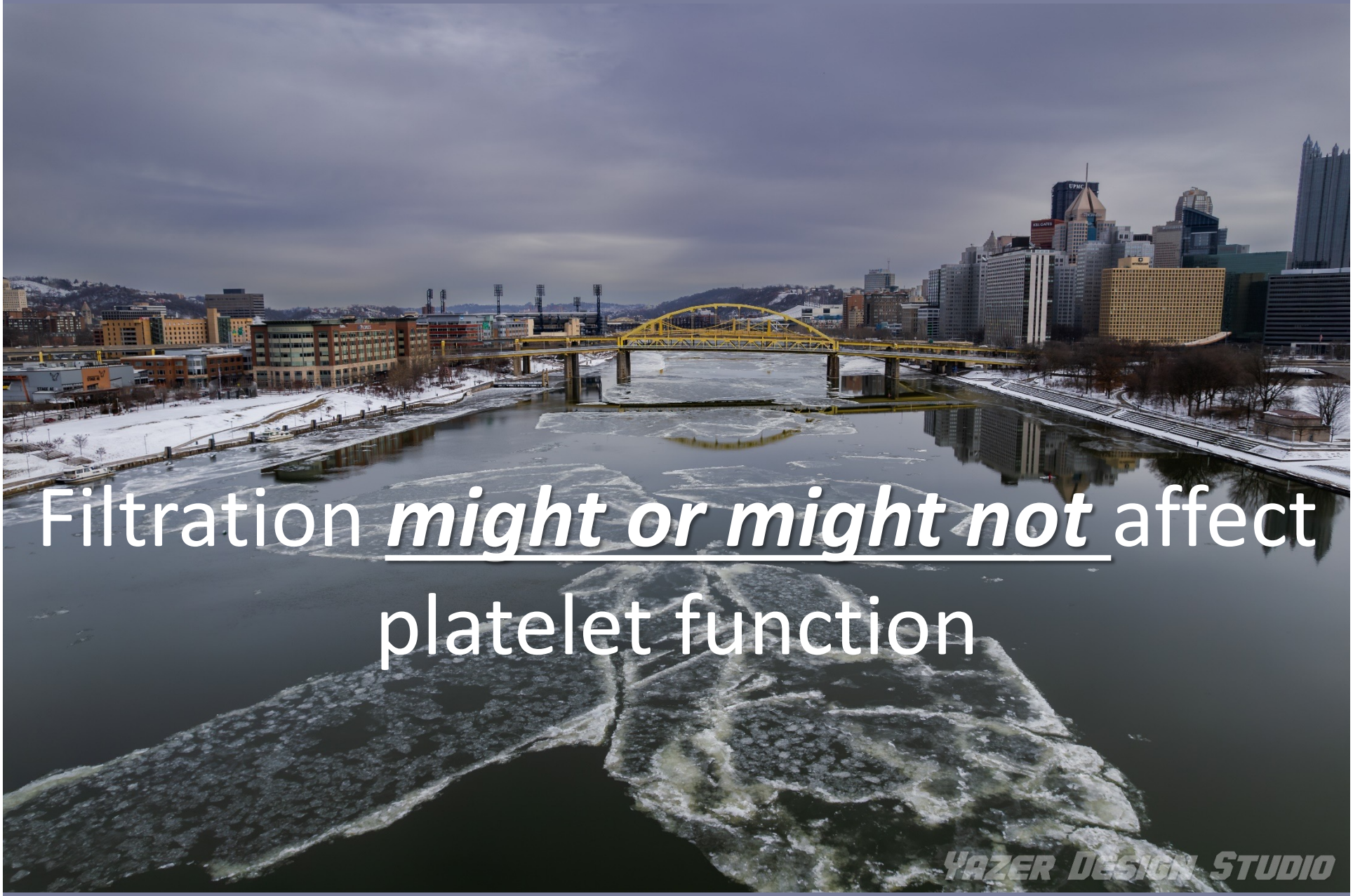
- Non-LR units can be kept cold for 24 hours
- LR has to occur within 8 hours
- Extra **16** hours could increase LTOWB donation





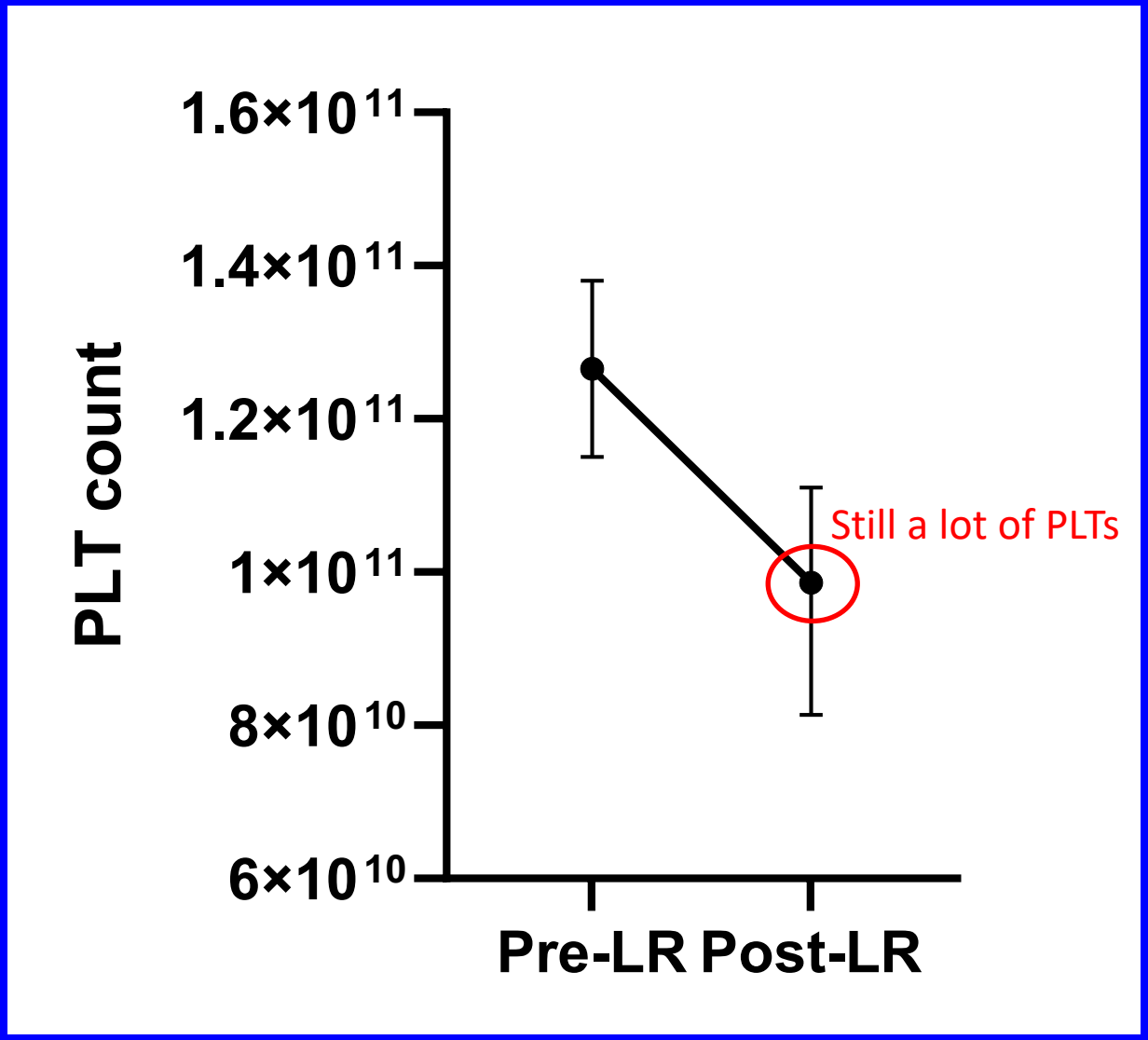
Yazer MH et al. *Transfusion* December 2024

Several problems with WB LR:2



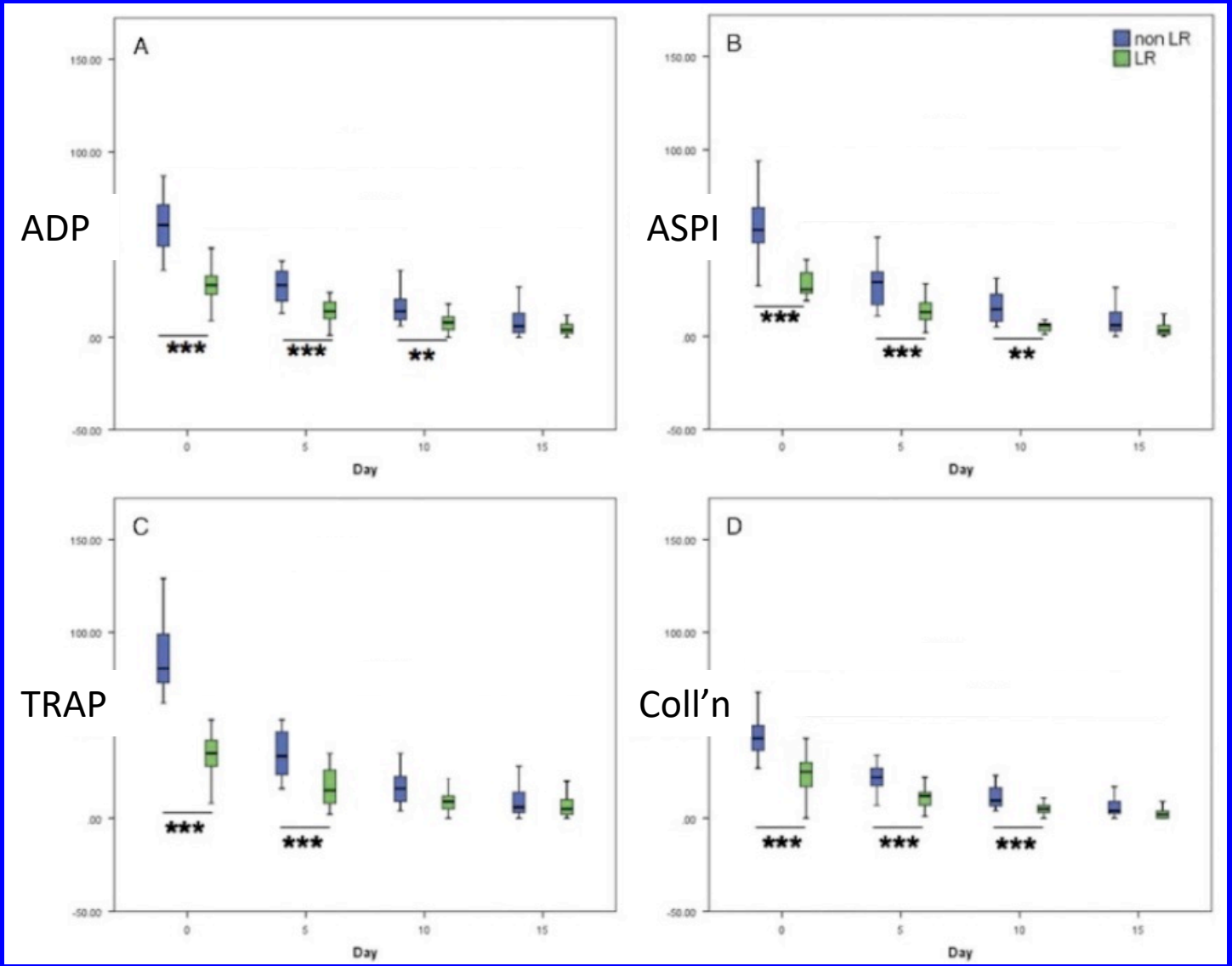
Filtration might affect PLT function

- PLT count: affected



Filtration might affect PLT function

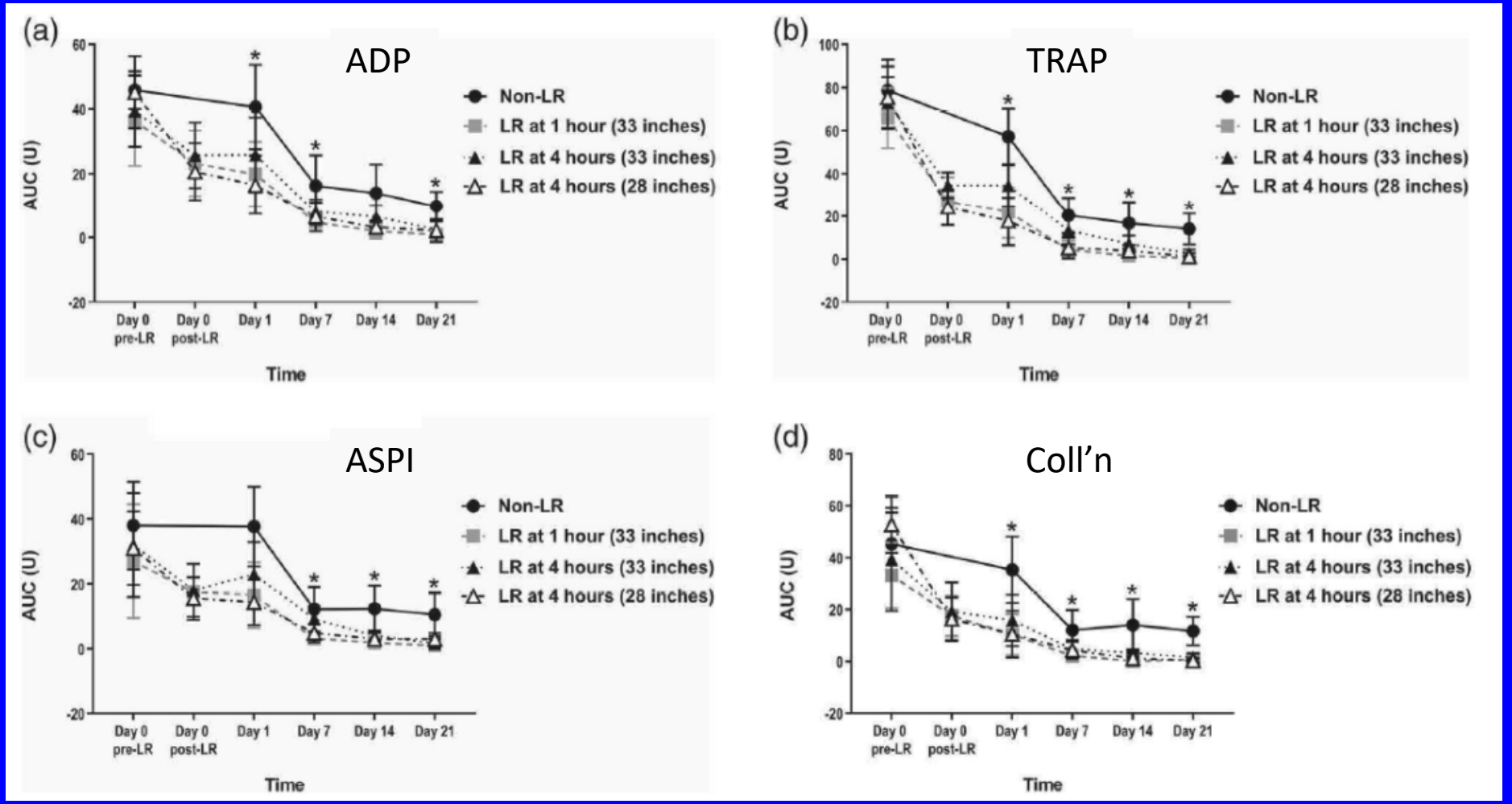
- PLT aggregometry: affected



Remy KE et al. *J Trauma Acute Care Surg* 2018;84:S104-S114

Filtration might affect PLT function

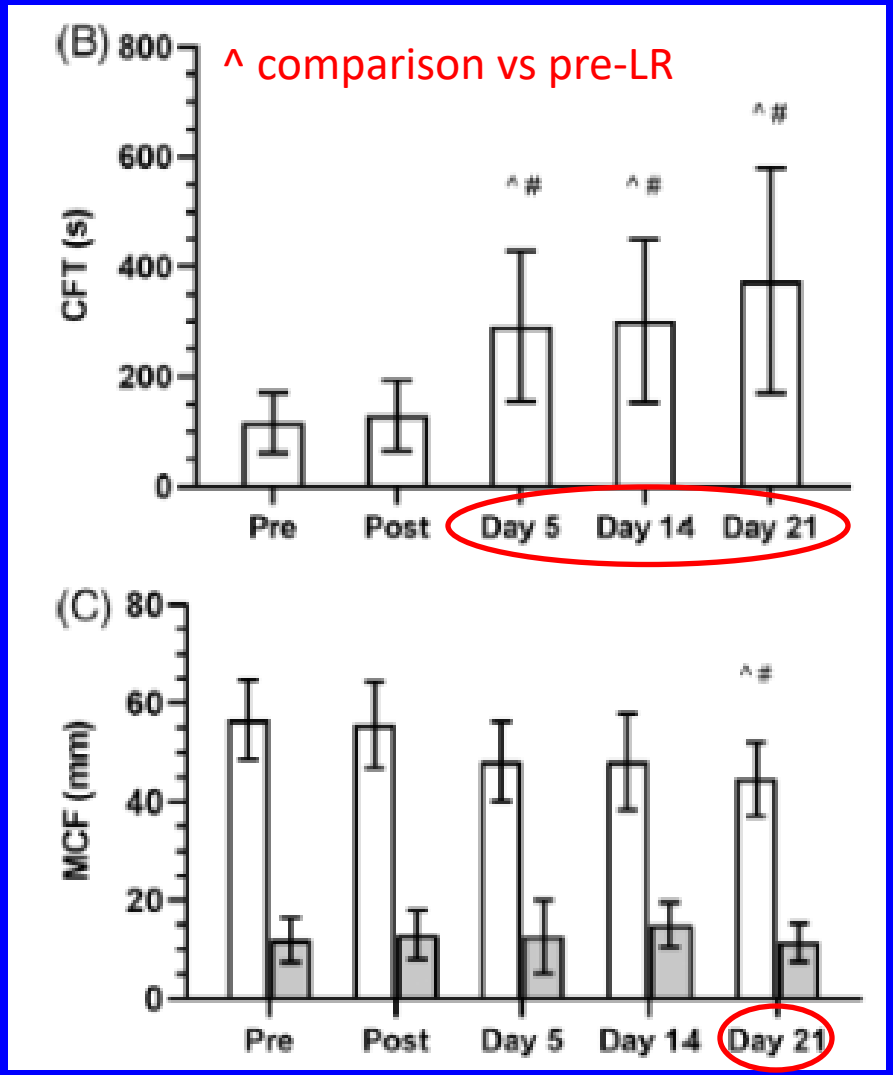
- PLT aggregometry: not affected



Morris MC et al. *Transf Med* 2019;29:351-357

Filtration might affect PLT function

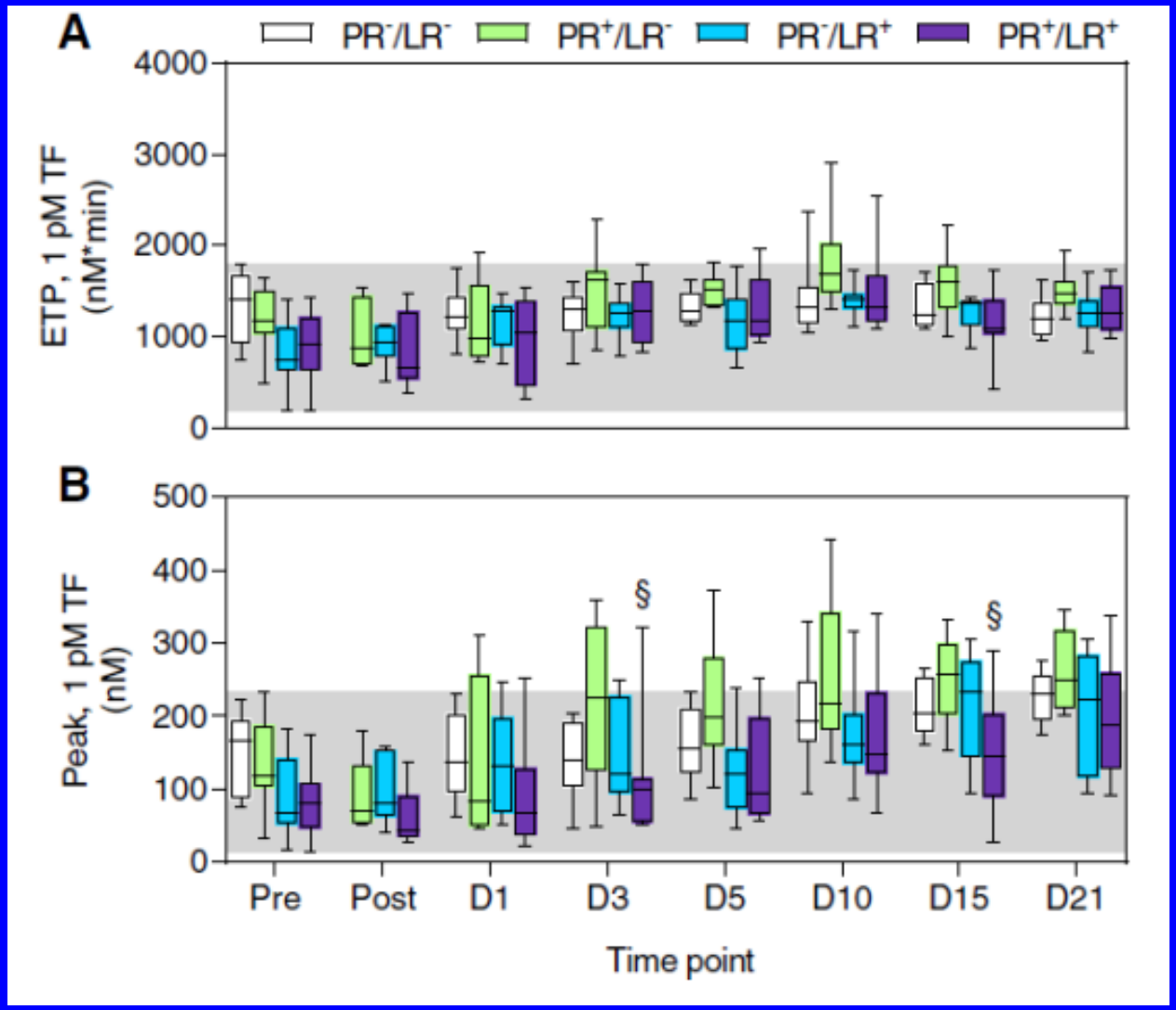
- Clot formation time, maximum clot firmness: affected



Rice J et al. *Transfusion* 2021;61:S90-S100

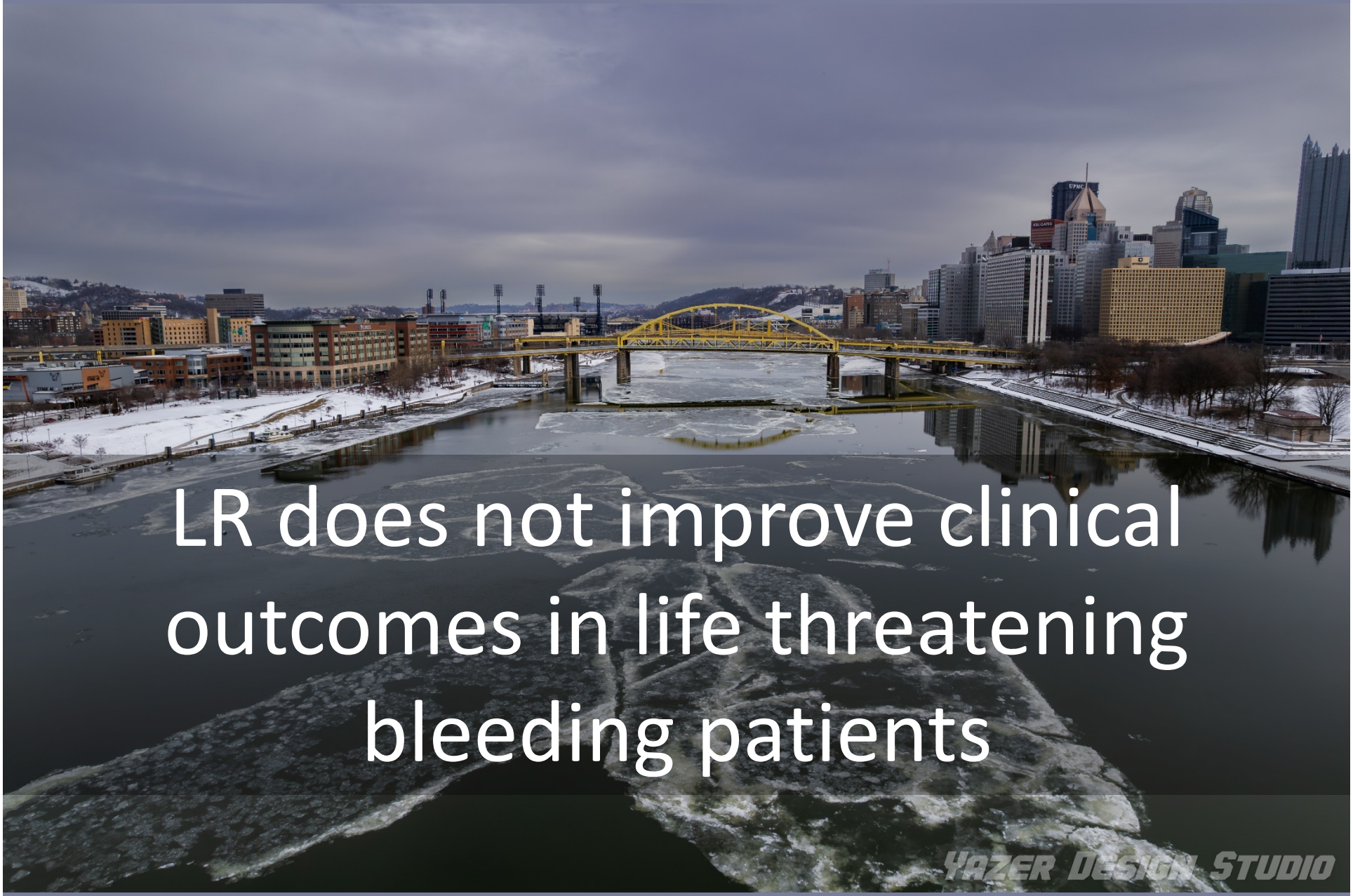
Filtration might affect PLT function

- Thrombin generation: not affected



Thomas KA et al. *Transfusion* 2019;59:1539-1548

Several problems with WB LR:3



LR not associated with improved survival

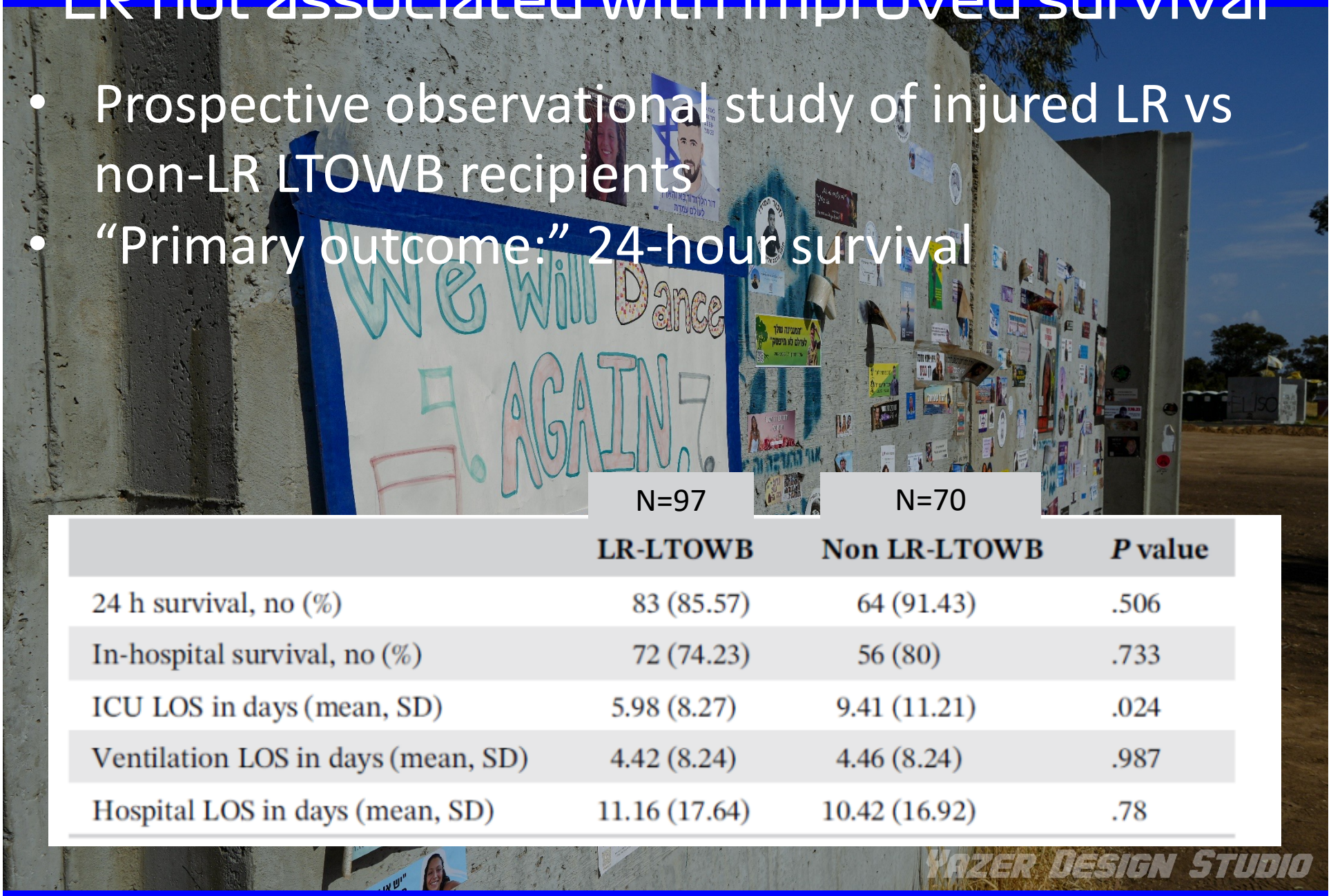
- Randomized trial of LR vs non-LR RBC transfusions in injured patients
- Evaluated infection within 28 days of randomization

Secondary analysis	Standard N = 136	Leukoreduced N = 132	RR	95% Confidence Interval
Early (≤72 hours from injury)				
ALI	31 (23)	32 (24)	1.06	(.69, 1.64)
ARDS	15 (11)	14 (11)	.96	(.48, 1.91)
Late (>72 hours from injury)				
ALI	28 (21)	24 (18)	.88	(.54, 1.44)
ARDS	26 (19)	24 (18)	.95	(.58, 1.57)
Hospital course (28 day)				
Requirement for mechanical ventilation	106 (78)	103 (78)	1.00	(.88, 1.14)
Hospital day of ALI diagnosis[a]	3 (2, 6)	3 (2, 5)		p = .6974
Number of ventilator-free days[b]	18 (11)	18 (11)		p = .8892 95% CI (−2.87, 2.49)

Watkins TR et al. *Crit Care Med* 2008;36:1493-1499
Nathens AB et al. *Shock* 2006;26:342-347

LR not associated with improved survival

- Prospective observational study of injured LR vs non-LR LTOWB recipients
- "Primary outcome:" 24-hour survival



	N=97 LR-LTOWB	N=70 Non LR-LTOWB	*P* value
24 h survival, no (%)	83 (85.57)	64 (91.43)	.506
In-hospital survival, no (%)	72 (74.23)	56 (80)	.733
ICU LOS in days (mean, SD)	5.98 (8.27)	9.41 (11.21)	.024
Ventilation LOS in days (mean, SD)	4.42 (8.24)	4.46 (8.24)	.987
Hospital LOS in days (mean, SD)	11.16 (17.64)	10.42 (16.92)	.78

Fadeyi EA et al. *Transfusion* 2020;60:2834-2840

THOR-AABB JOINT WORKING GROUP conclusion on LR for life threating bleeding

For clinical programs that use LTOWB for treating patients with life threatening hemorrhage, the data do not support requiring the LTOWB to be leukoreduced. The leukoreduction of LTOWB for patients with life threatening hemorrhage could be considered optional unless its use is mandated by local or national regulations

Association for the Advancement of Blood & Biotherapies

THOR TRAUMA HEMOSTASIS & OXYGENATION RESEARCH

Yazer MH et al. *Transfusion* 2024;64:2391-2399

Not everyone agrees

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COMMENTARY

TRANSFUSION

Eliminating leukocyte reduction for whole blood: Is it premature to consider this paradigm-changing practice?

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Transfusion 2025;65:375-378

Apply the same standard, please

- Editorial suggesting that because we do not have RCT data showing superiority of (presumably non-LR) LTOWB to (presumably LR) CT, we should use the LR product

- SCT
- AML
- Colorectal surgery
- Cardiac surgery

The commentary from Yazer and colleagues conflicts with contemporary hemovigilance and blood safety standards to accommodate a sense of urgency around the implementation of LTOWB in routine civilian settings. In the absence of unequivocal evidence, just as there is biological rationale—but not RCT data—for the superiority of LTOWB compared with component therapy, the same currently exists for the use of LR in trauma resuscitation. Indeed, most evidence to date regarding LR in a wide variety of clinical settings supports the hypothesis that LR in LTOWB, with either a platelet sparing or nonplatelet sparing filter, reduces harm in many trauma patients with serious hemorrhage.

- PPH?
- GI bleeding?
- ANY other surgery?
- AAA?

  Etc…

Adkins et al. *Transfusion* 2025;65:375-378

Conclusions

- If you are obliged to do LR, do LR
- If you are not obliged, ask yourself why you are doing LR?
- Probably minimal harm in LR, probably minimal harm in not LR
- Would non-LR improve your inventory? Simplify your collections program?

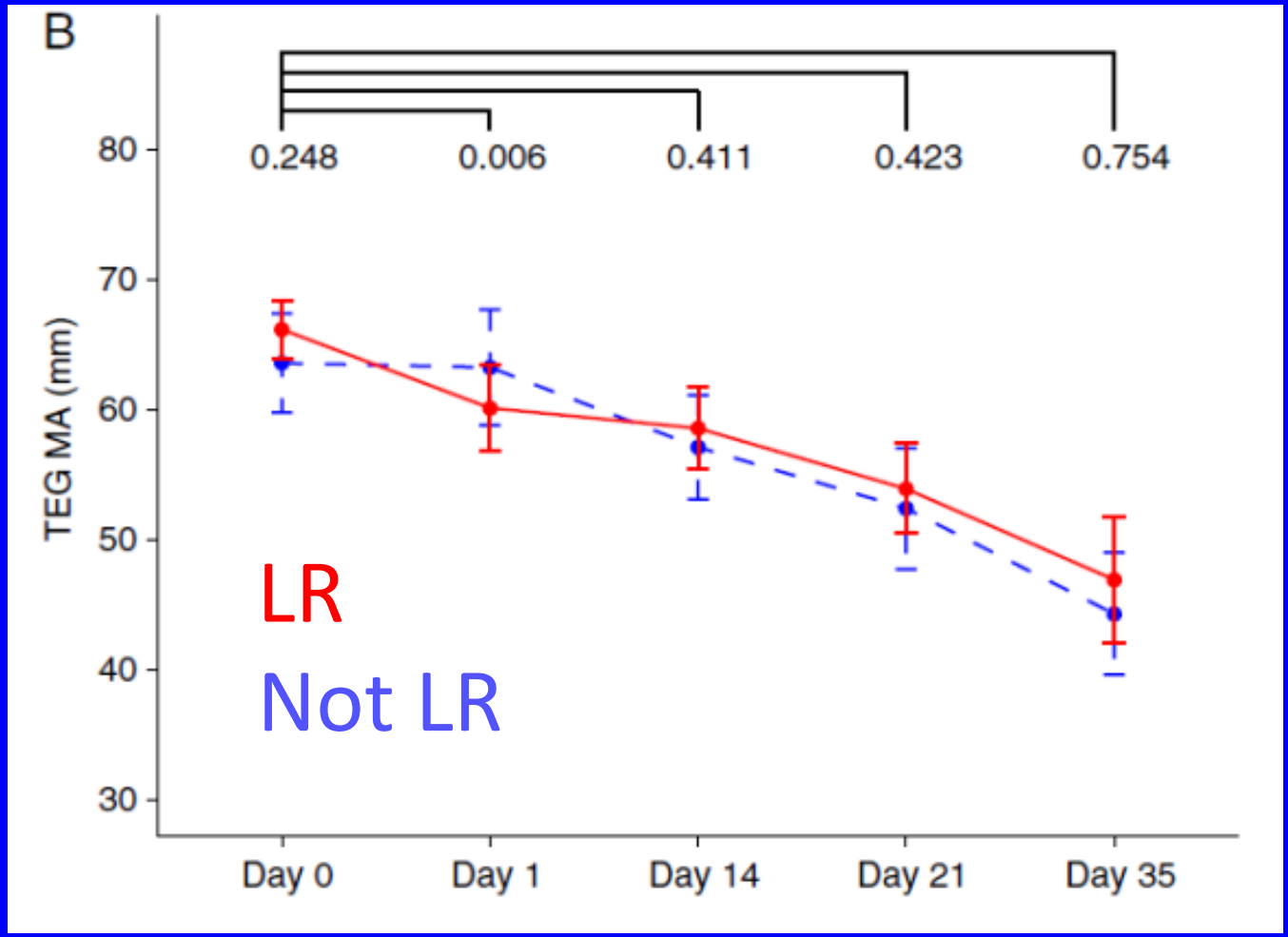
Thanks a lot!

Another possible problem with LR

- LTOWB storage to day 35

Effect of extended storage on PLT

- TEG maximum amplitude (MA): clearly worse at day 35



Sivertsen J et al. *Transfusion* 2020;60:1042-1049