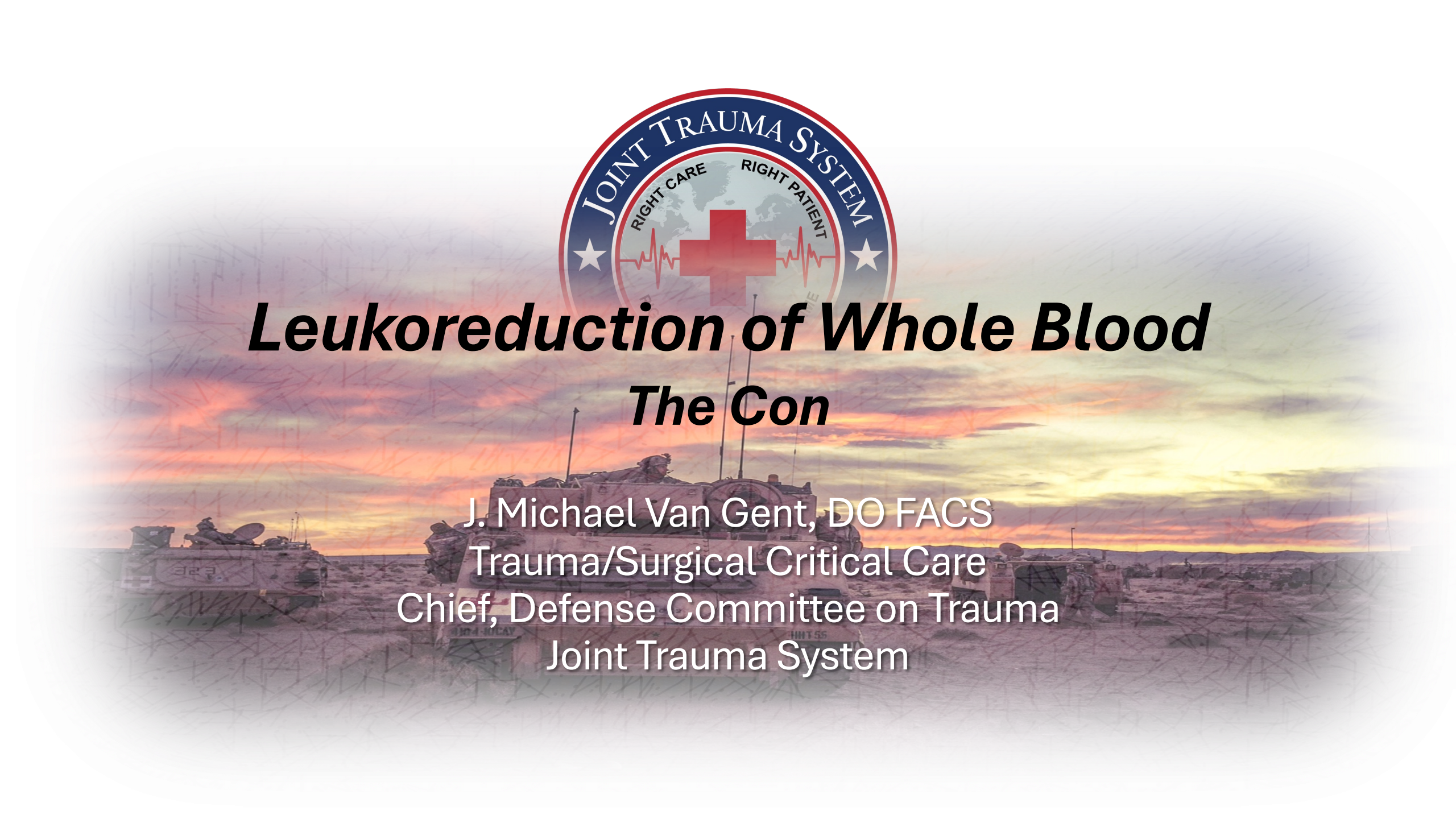


# *Leukoreduction of Whole Blood*

## *The Con*

J. Michael Van Gent, DO FACS
Trauma/Surgical Critical Care
Chief, Defense Committee on Trauma
Joint Trauma System

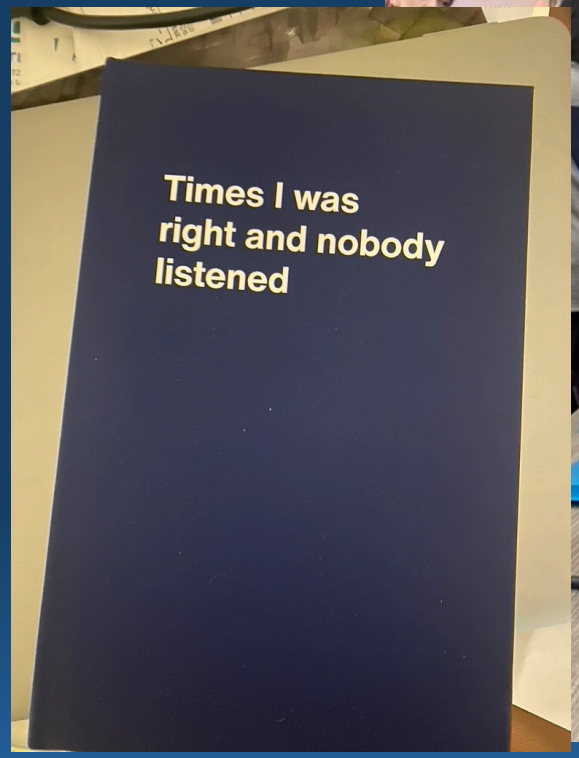
# Disclosures

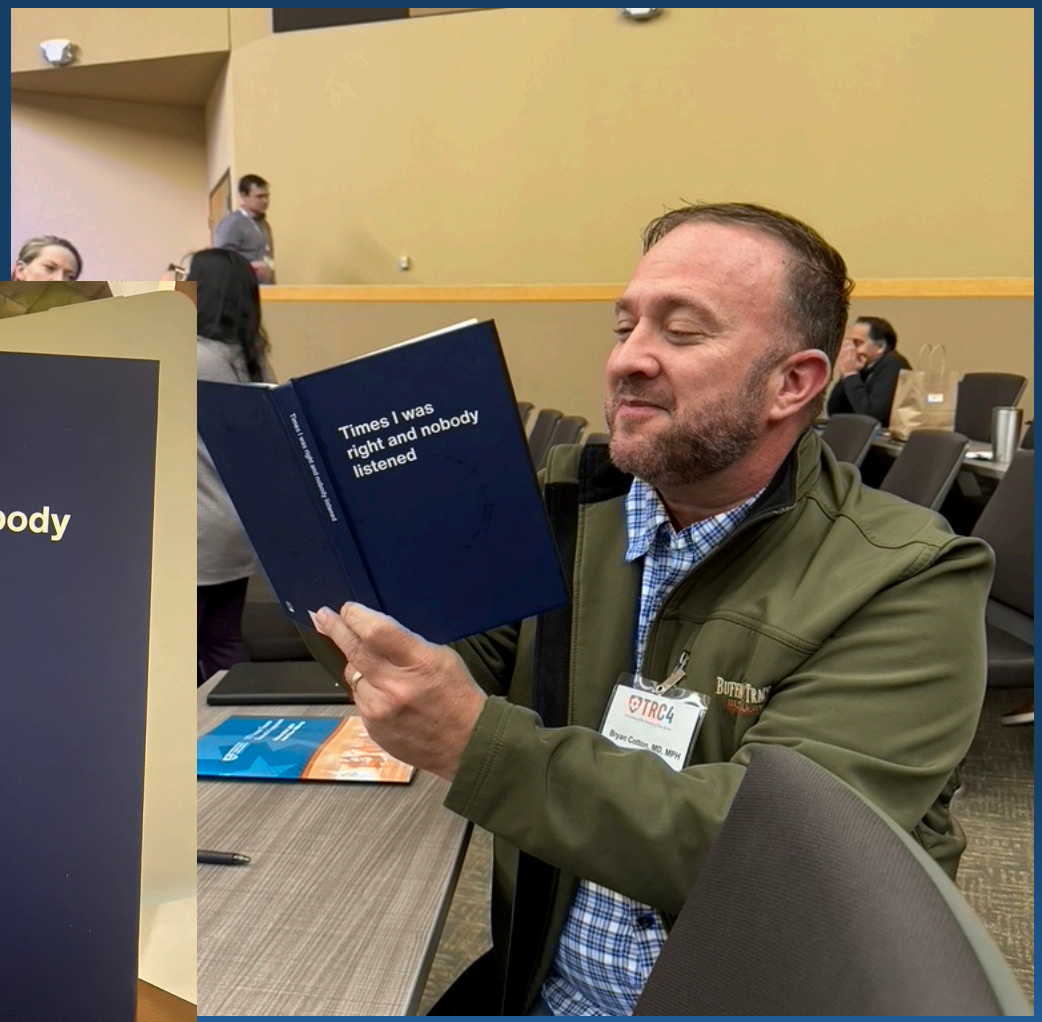
The views expressed herein are those of the author and do not necessarily reflect the official policy or position of the Defense Health Agency, the Department of Defense, nor any agencies under the U.S. Government

Although the DoD AGREES with me…

# I'm Not Bryan Cotton

- But he approves of this message…



**Blood is for bleeding.**
**Salt water is for cooking pasta.**

- PHIL SPINELLA, MD FCCM

# Why Leukoreduce Whole Blood?

**Reduce:**

- TRALI
- Febrile reactions
- Transfusion-Transmitted Diseases
  - CMV, HTLV, prions

- Maybe Reduces:
  - HLA alloimmunization
  - TA-GvHD

**Effects of whole blood leukoreduction on platelet function and hemostatic parameters**

M. C. Morris,[1] R. Veile,[1] L. A. Friend,[1] D. Oh,[2,3] T. A. Pritts,[1] W. C. Dorlac,[4] P. C. Spinella[5] & M. D. Goodman[1]

Leukoreduction (LR) is thought to be an additional step that could improve safety in the use of whole blood. LR is able to reduce human leukocyte antigen (HLA) alloimmunization, febrile reactions and viral transmission. However, whole blood platelet function has been shown to decrease over time during storage (Pidcoke *et al.*, 2013). The effects on platelet quantity and mass, function and hemostatic performance following LR using an FDA-approved platelet-sparing filter at various heights are unknown. We aimed to examine the effect of *in vitro* LR on whole

# Reduces TRALI?

Cochrane Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

## Leukoreduction for the prevention of adverse reactions from allogeneic blood transfusion

| | NLR | LR | | |
|---|---|---|---|---|
| **TRALI**<br>Follow-up: mean 28 days | **Study population** | | **RR 0.96**<br>(0.67 to 1.36) | 1864<br>(1 study) |
| | **63 per 1000** | **61 per 1000**<br>(42 to 86) | | |

# Shorter Shelf Life

THOR 2018

## Preparation of leukoreduced whole blood for transfusion in austere environments; effects of forced filtration, storage agitation, and high temperatures on hemostatic function

**Joar Sivertsen, Hanne Braathen, Turid Helen F. Lunde, MSc, Philip C. Spinella, MD, Warren Dorlac, MD, Geir Strandenes, MD, Torunn O. Apelseth, PhD, Tor A. Hervig, PhD,** *and* **Einar K. Kristoffersen, PhD**, *Bergen, Norway*

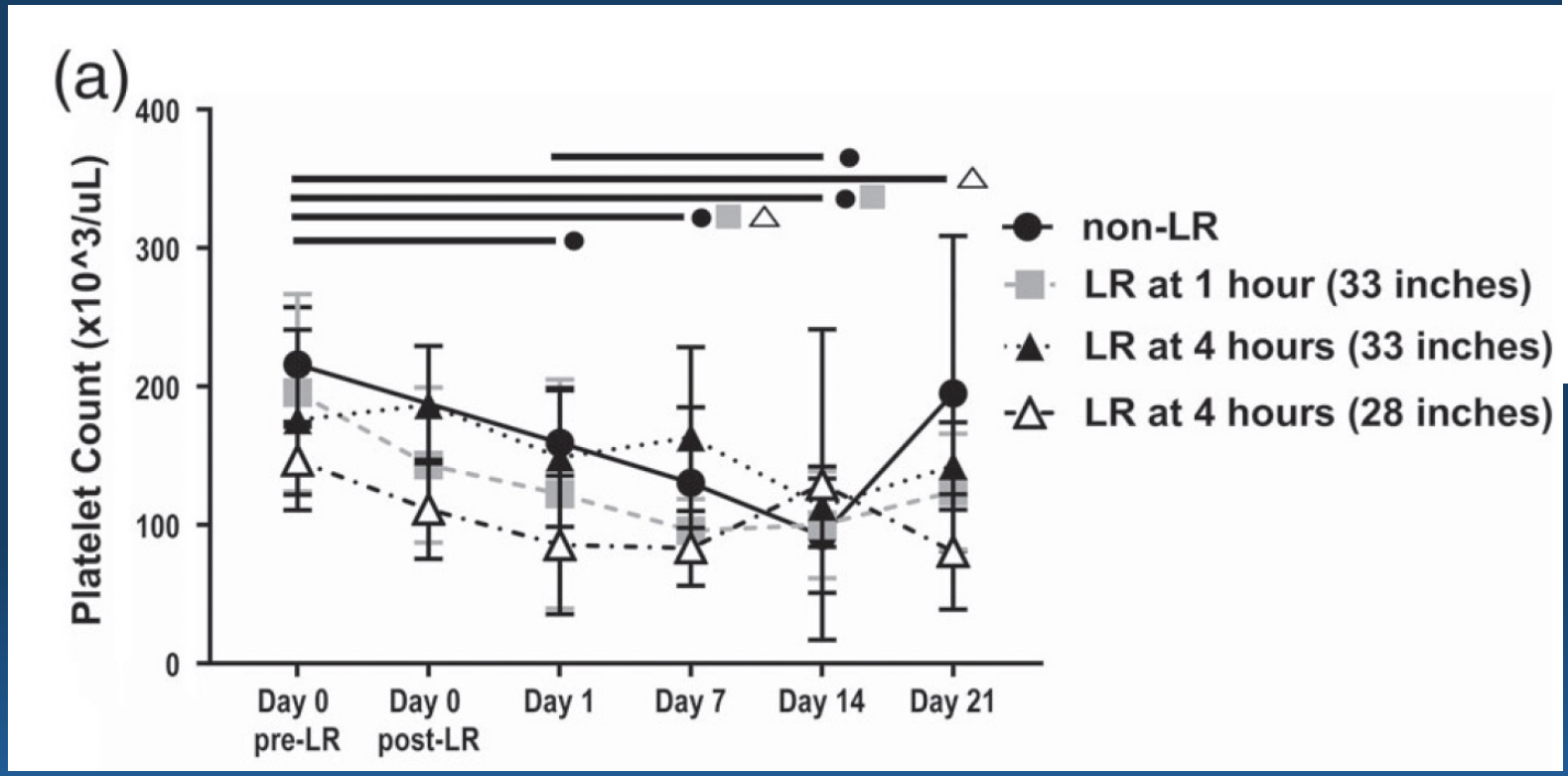

However, there is presently no collection set commercially available with an in-line platelet-sparing filter and CPDA-1 as additive. That said, the demand for WB is growing and if studies show a benefit, manufacturers may respond.

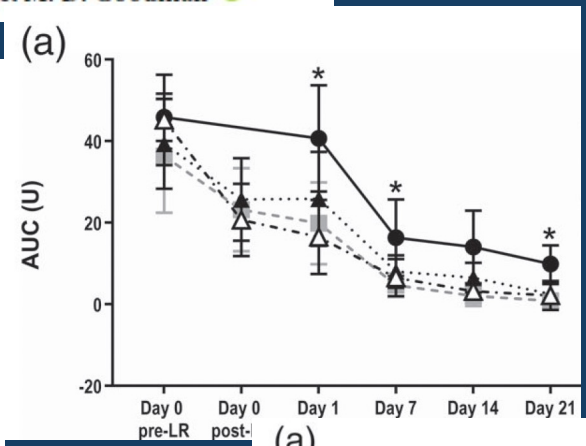
**Storage = 21 vs 35 days**

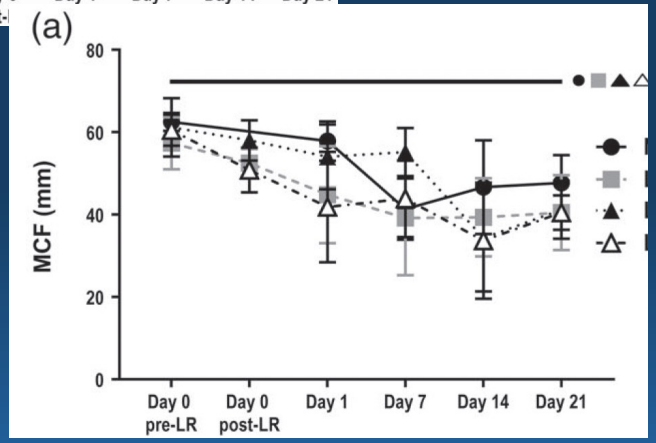
# Platelets are the collateral damage

## Effects of whole blood leukoreduction on platelet function and hemostatic parameters

M. C. Morris,[1] R. Veile,[1] L. A. Friend,[1] D. Oh,[2,3] T. A. Pritts,[1] W. C. Dorlac,[4] P. C. Spinella[5] & M. D. Goodman[1]

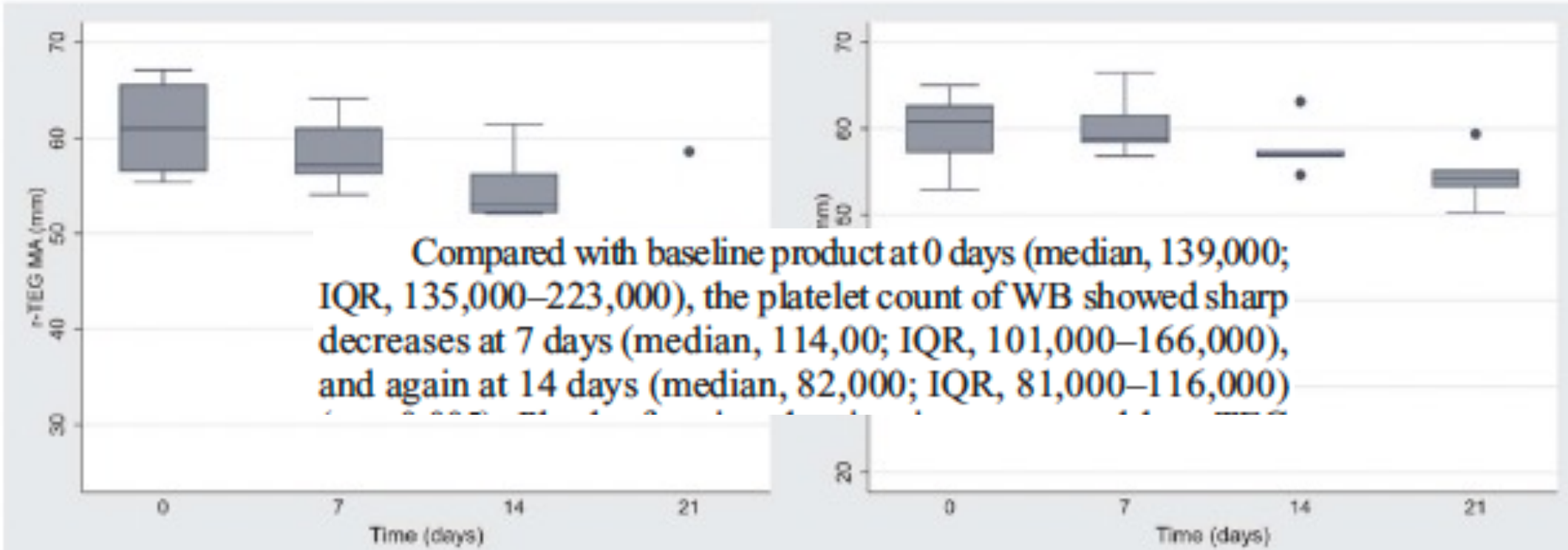


# Hemostatic potential of cold-stored non-leukoreduced whole blood over time: An assessment of platelet function and thrombin generation for optimal shelf life

**Scott Assen, MD, Jessica Cardenas, PhD, Mitchell George, MD, Yao-Wei Wang, PhD, Charles E. Wade, PhD, David Meyer, MD, MS,** *and* **Bryan A. Cotton, MD, MPH**, *Houston, Texas*




Compared with baseline product at 0 days (median, 139,000; IQR, 135,000–223,000), the platelet count of WB showed sharp decreases at 7 days (median, 114,00; IQR, 101,000–166,000), and again at 14 days (median, 82,000; IQR, 81,000–116,000)

# Platelets are the collateral damage

Platelet function of whole blood is the most age-dependent factor in hemostatic potential…

## Why start out at a disadvantage?

# Warm Fresh Whole Blood Is Independently Associated With Improved Survival for Patients With Combat-Related Traumatic Injuries

*Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Alec C. Beekley, MD, and John B. Holcomb, MD*

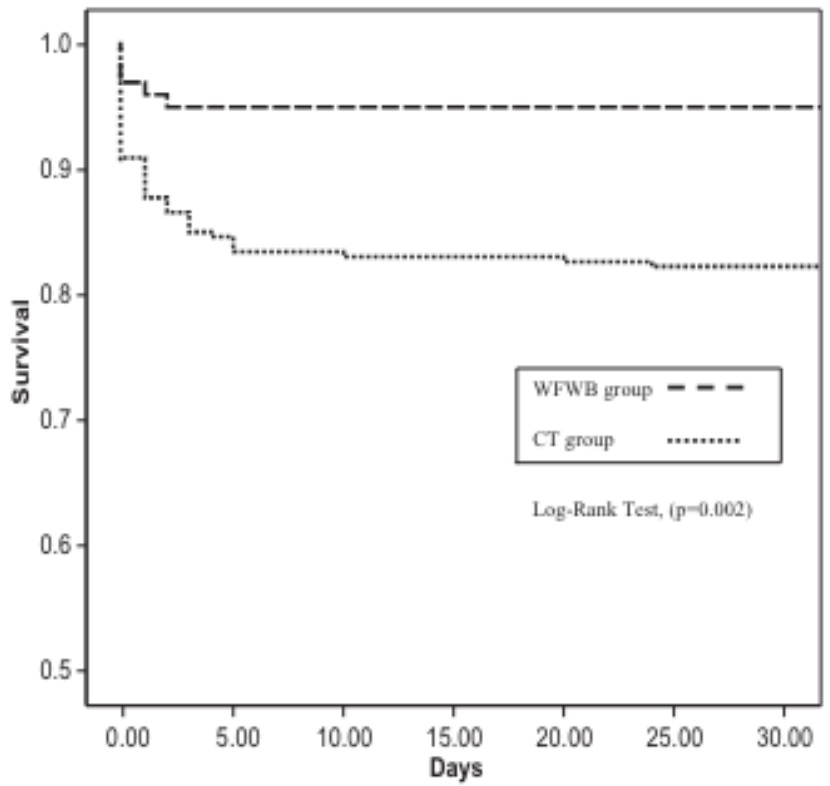



**Fig. 1.** *Kaplan-Meier curve of 30-day survival according to study group.*

The clinical effects of transfusing functional white blood cells are unknown in this population. There is the potential that the transfusion of increased amounts of WBCs may promote inflammatory injury. Transfusion-associated microchimerism (TA-MC) has been reported to be associated with the transfusion of viable white blood cells in RBC units of decreased storage age in patients with trauma.[53] The clinical significance of this phenomenon has not been clearly defined.[53] The development of transfusion-associated graft versus host disease or any other immunologic disorder has not been reported in patients with trauma as a result of TA-MC. Transfusion reactions were similar in a recent report comparing combat casualty patients transfused WFWB to those who were not.[37] In addition, the use of prestorage leukoreduced RBCs in patients with trauma has not been demonstrated to improve outcomes.[54,55] Contrary to the concern that the transfusion of fresh WBCs may be detrimental, it may also be possible that the transfusion of functional WBCs from a healthy volunteer may actually improve modulation of the inflammatory system that is both overactive and underactive after traumatic injury.[56] Our results that WFWB

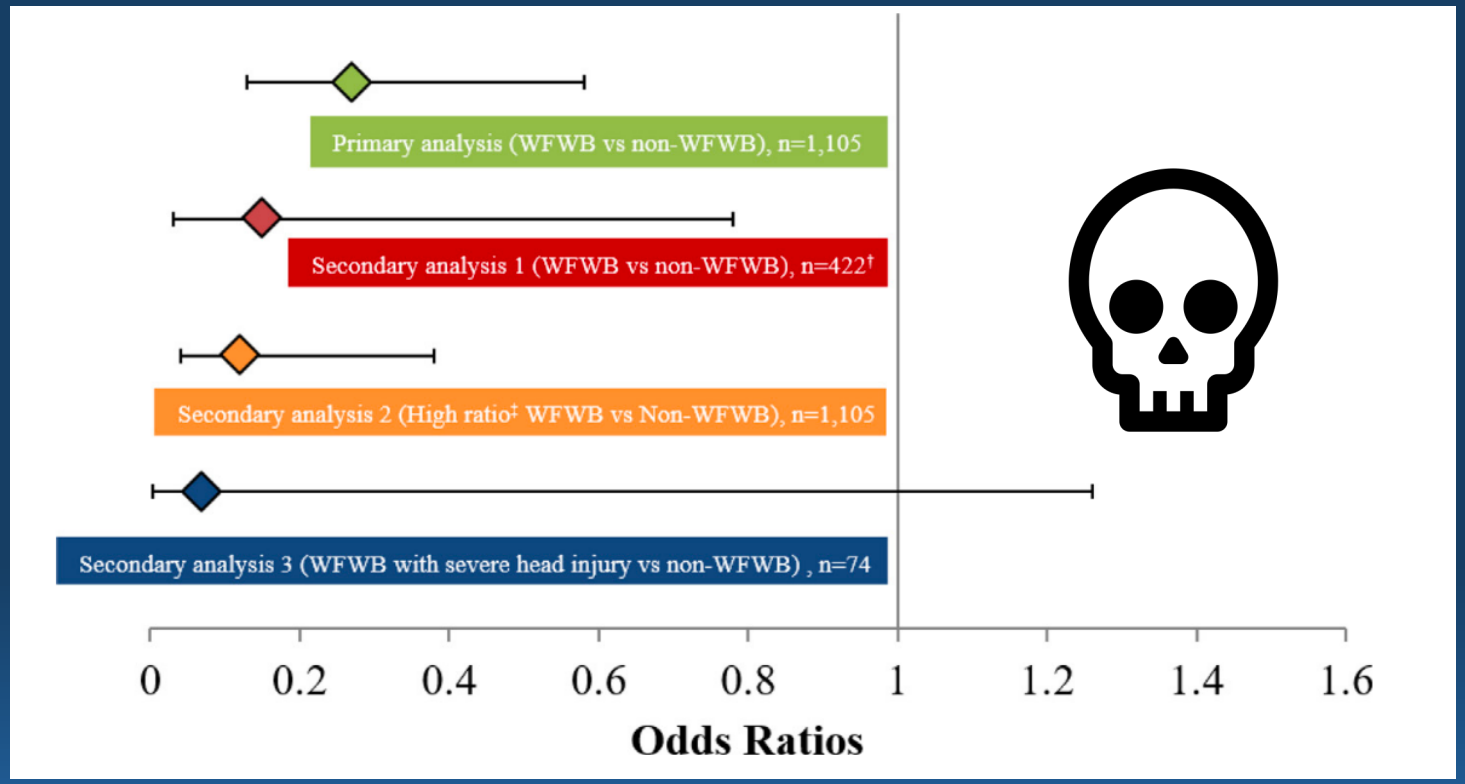
Whole blood at the tip of the spear: A retrospective cohort analysis of warm fresh whole blood resuscitation versus component therapy in severely injured combat casualties

Jennifer M. Gurney, MD, FACS[a,b,c,*], Amanda M. Staudt, PhD[d], Deborah J. del Junco, PhD[b], Stacy A. Shackelford, MD, FACS[b,c], Elizabeth A. Mann-Salinas, PhD[a,b], Andrew P. Cap, PhD, MD[a,c], Philip C. Spinella, MD[e], Matthew J. Martin, MD, FACS[c,f]

**WFWB**

**Adjusted**

**WFWB + TBI**



# Impact of Incorporating Whole Blood into Hemorrhagic Shock Resuscitation: Analysis of 1,377 Consecutive Trauma Patients Receiving Emergency-Release Uncrossmatched Blood Products

Jason B Brill, MD, Brian Tang, BS, Gabrielle Hatton, MD, Krislynn M Mueck, MD, C Cameron McCoy, MD, Lillian S Kao, MD, MS, FACS, Bryan A Cotton, MD, MPH, FACS

| | Unweighted analysis | | Weighted analysis | |
|---|---|---|---|---|
| **30-day survival** | **Odds ratio (95% CI)** | **p Value** | **Odds ratio (95% CI)** | **p Value** |
| WB group | 4.10 (2.22-7.45) | <0.001 | 1.59 (1.28-1.98) | <0.001 |
| Age, per year | 0.97 (0.96-0.98) | 0.001 | 0.99 (0.98-0.99) | <0.001 |
| Male sex | 0.46 (0.24-0.87) | 0.018 | 0.77 (0.60-0.98) | 0.04 |
| ISS, per point | 0.93 (0.92-0.95) | <0.001 | 0.95 (0.94-0.96) | <0.001 |
| Scene SBP, per mmHg | 1.00 (0.99-1.01) | 0.286 | 1.009 (1.006-1.012) | <0.001 |
| Arrival lactate, per mmol/L | 0.82 (0.76-0.88) | <0.001 | 0.89 (0.87-0.92) | <0.001 |

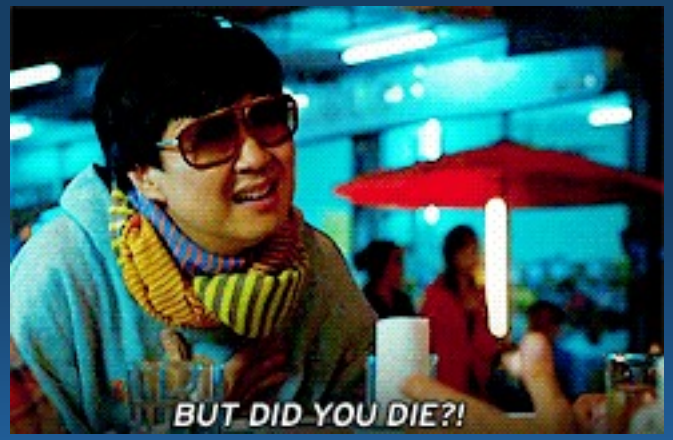
CI, confidence interval; ISS, Injury Severity Score; SBP, systolic blood pressure; WB, whole blood arm.

| | | | |
|---|---|---|---|
| TRALI, % | 0.14 | 0.45 | 0.271 |
| TACO, % | 0.14 | 0.00 | 0.385 |
| Transfusion reaction, % | 0.43 | 0.00 | 0.128 |

**Table 6.** Multivariable Analyses Evaluating the Impact of Low-Titer Group O Whole Blood on 24-Hour Blood Product Use Among All Patients

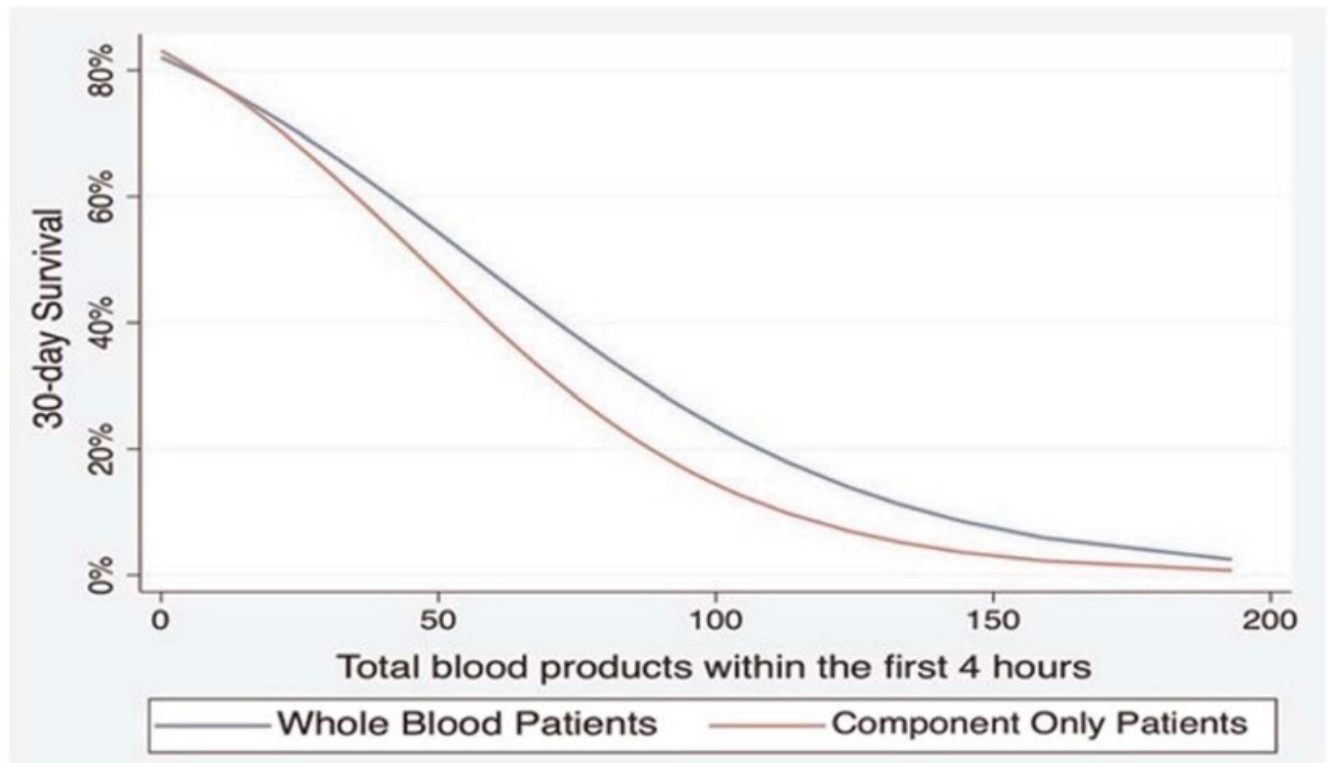
| | Unweighted analysis | | Weighted analysis | |
|---|---|---|---|---|
| **24-hour blood product use** | **Rate ratio (95% CI)** | **p Value** | **Rate ratio (95% CI)** | **p Value** |
| Whole blood group | 0.38 (0.21-0.70) | 0.002 | 0.93 (0.91-0.96) | <0.001 |
| Age, per year | 1.00 (0.99-1.02) | 0.602 | 0.996 (0.995-0.997) | <0.001 |
| Male sex | 1.80 (0.98-3.26) | 0.055 | 1.22 (1.18-1.26) | <0.001 |
| ISS, per point | 1.07 (1.04-1.09) | <0.001 | 1.023 (1.022-1.024) | <0.001 |
| Scene SBP, per mmHg | 0.99 (0.99-1.01) | 0.639 | 0.998 (0.998-0.991) | <0.001 |
| Arrival lactate, per mmol/L | 1.12 (1.02-1.25) | 0.019 | 1.038 (1.036-1.039) | <0.001 |

CI, confidence interval; ISS, Injury Severity Score; SBP, systolic blood pressure; WB, whole blood arm.



# The reports of my death are greatly exaggerated: An evaluation of futility cut points in massive transfusion

**Thomas W. Clements, MD, FRCSC, Jan-Michael Van Gent, DO, FACS, David E. Lubkin, MD, Michael W. Wandling, MD, FACS, David E. Meyer, MD, FACS, Laura J. Moore, MD, FACS,** *and* **Bryan A. Cotton, MD, FACS**, *Houston, Texas*




# Prehospital whole blood reduces early mortality in patients with hemorrhagic shock

Maxwell A. Braverman[1] | Alison Smith[1] | Douglas Pokorny[1] | Benjamin Axtman[1] | Charles Patrick Shahan[1] | Lauran Barry[1] | Hannah Corral[1] | Rachelle Babbitt Jonas[1] | Michael Shiels[2] | Randall Schaefer[3] | Eric Epley[3] | Christopher Winckler[4] | Elizabeth Waltman[5] | Brian J. Eastridge[1] | Susannah E. Nicholson[1] | Ronald M. Stewart[1] | Donald H. Jenkins[1]

| | PHT ($n = 58$) | NT ($n = 156$) | $p$-value |
|---|---|---|---|
| Median prehospital nadir SBP (IQR) | 75 (62–83) | 74 (66–82) | .91 |
| Median prehospital HR (IQR) | 113 (90–128) | 93 (79–125) | *.03* |
| Median prehospital SI (IQR) | 1.5 (1.2–2.0) | 1.4 (1.1–1.8) | .051 |
| Median arrival SBP, mmHg (IQR) | 92 (81–114) | 86 (77–100) | .07 |
| Median arrival HR, mmHg (IQR) | 113 (92–130) | 106 (83–128) | .87 |
| Median arrival SI (IQR) | 1.2 (0.87–1.48) | 1.21 (0.9–1.5) | .66 |
| Median Delta SI (IQR) | −0.38 (−0.08 to −0.72) | −0.18 (0.02 to −0.48) | .04 |
| Death in ED, % ($n$) | 0.0 (0) | 7.1 (11) | *.04* |
| Death in 6 h, % ($n$) | 5.3 (3) | 14.1 (22) | .08 |
| Death in 24 h, % ($n$) | 17.2 (10) | 23.1 (36) | .36 |
| Hospital death, % ($n$) | 13.8 (8) | 25 (39) | .08 |
| CAT3+ transfusion requirement, % ($n$) | 53.4 (31) | 60.3 (94) | .37 |
| MT (>10 U in 24 h), % ($n$) | 61.5 (16) | 48.7 (75) | .23 |
| Median arrival transfusion volume, ml (IQR) | 1300 (0–2000) | 1975 (1000–3175) | *<.01* |
| Median LOS transfusion volume, ml, (IQR) | 2825 (1550–5500) | 2000 (1300–4000) | .048 |

# Texas and the DoD don’t Leukoreduce LTOWB…



## So it must be the right answer

# THOR-AABB Working Party Recommendations for a Prehospital Blood Product Transfusion Program

Mark H. Yazer, Philip C. Spinella, Eric A. Bank, Jeremy W. Cannon, Nancy M. Dunbar, John B. Holcomb, Bryon P. Jackson, Donald Jenkins, Michael Levy, Paul E. Pepe, Jason L. Sperry, James R. Stubbs & Christopher J. Winckler

There is no evidence that leukoreduction of RBCs (27–30) or LTOWB (31) improves outcomes in injured patients; the role of leukoreduction in other patient groups that might require prehospital transfusions has not been well studied

# Summary

- **Leukoreduction:**
  - Increases cost (filter + shorter shelf life)
  - Reduces shelf life
  - Maybe reduces TRALI?
  - Reduces platelet count, aggregation and activity
    - Enough to matter?
  - NLR LTOWB data from San Antonio, Houston, and the DoD show an excellent safety profile and survival benefit

# Conclusions

- For life-threatening hemorrhage, no data to support LR over NLR
- For Rural areas and the Military Health System NLR WB has benefits over LR WB
  - Logistical Constraints (distribution time frame + lack of stored platelets)
  - Longer shelf life + higher platelet count and improved function
    - Especially when accounting for functional decline as the product ages
- LR should be considered in higher risk populations where there is a paucity of data
  - neonates, transplant, oncology, low HLA haplotype diversity populations (Japanese)