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LTOWB DATA REVIEW

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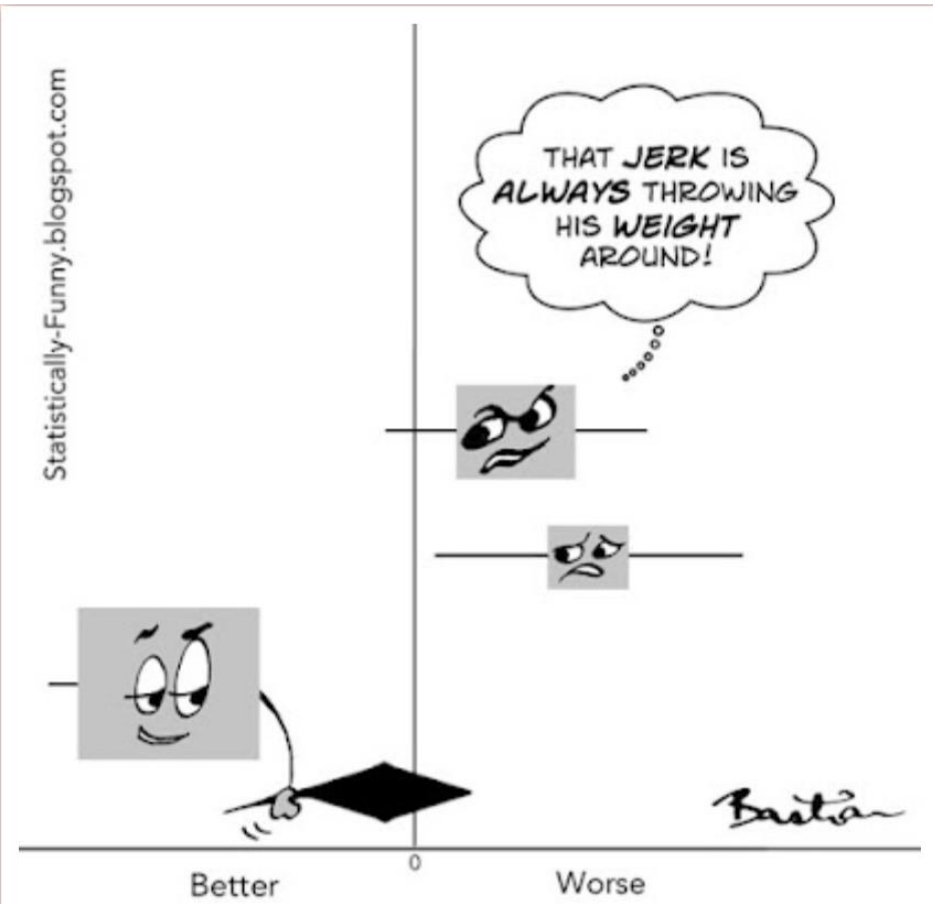
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University of Pittsburgh



OVERVIEW

- New studies (2023-2024)
- Concepts:
 - Donor Exposures
 - Dose Effect
 - Timing
 - Cost
 - Survival

Statistically-Funny.blogspot.com

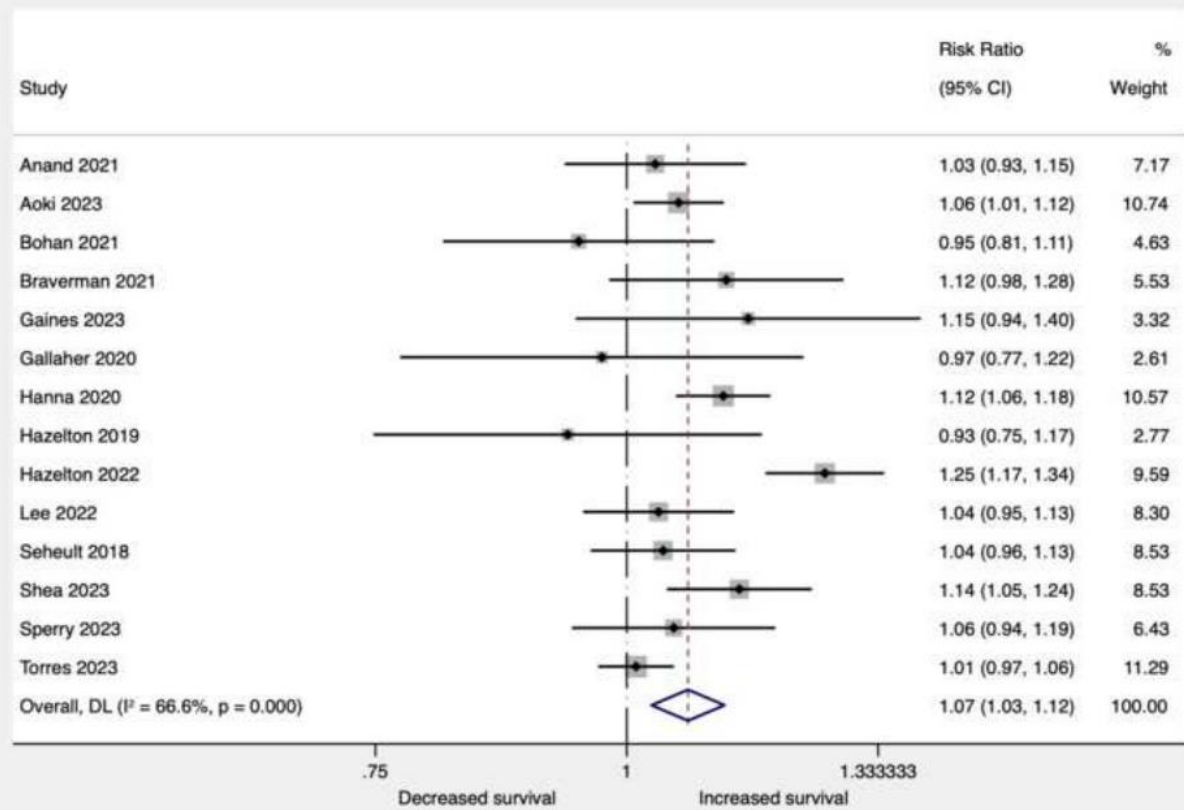


SURVIVAL

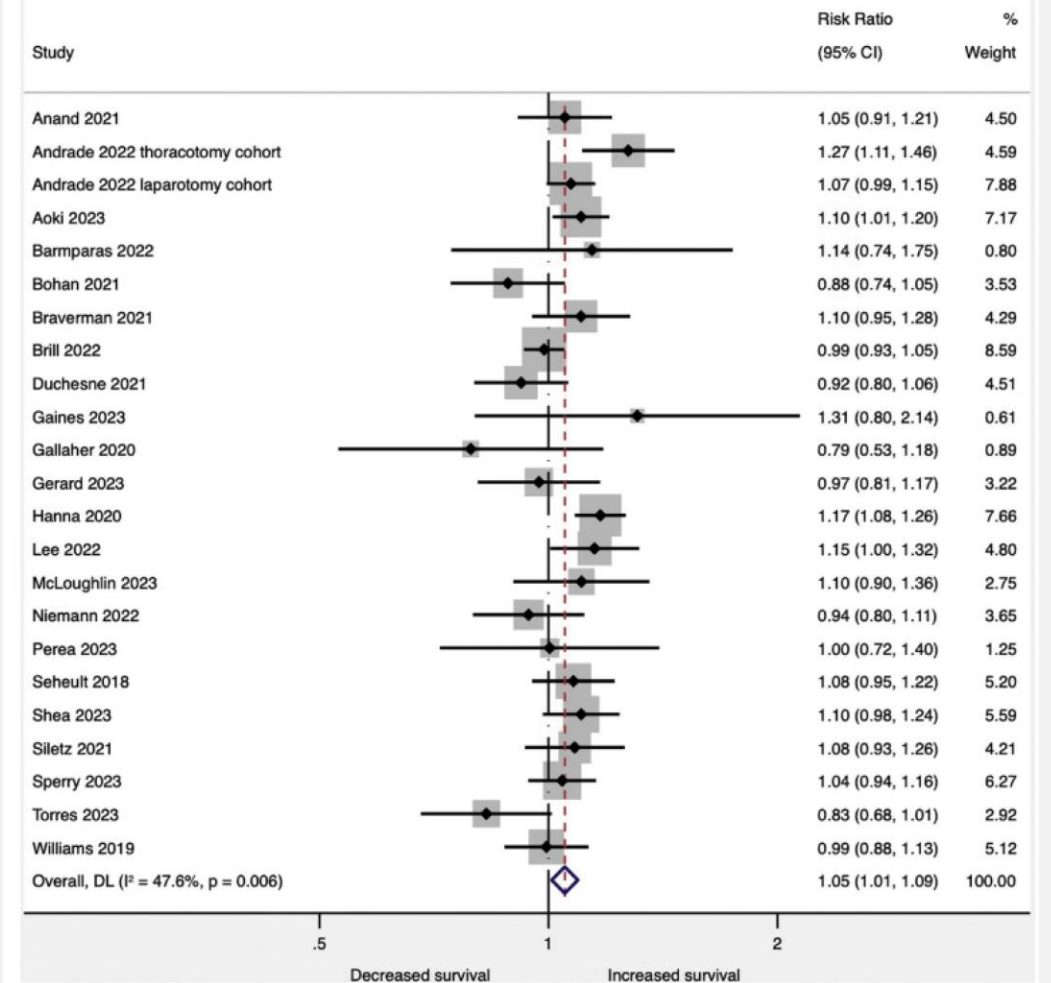
MORGAN ET AL, CRIT CARE MED JULY 2024

- Adults and children
- Inception through Dec 2023
- PubMed, CINAHL, and Web of Science
- Excluded: military, non-LTOWB product type
- 14 studies reported early (<24h) mortality and 22 studies reported late (28d, 30d, in-hospital) mortality

Early mortality



Late mortality



Forest plot of studies reporting late (28-d, 30-d, or in-hospital) survival rates in trauma patients who received low-titer group O whole blood (LTOWB) compared with component therapy (n = 54,762). LTOWB was significantly associated with improved late survival compared with component therapy (relative risk [95% CI] = 1.05 [1.01–1.09], p = 0.014). DL = DerSimonian and Laird.

Compared to CT, LTOWB was associated with improved:
 24-hour survival (RR [95% CI] = 1.07 [1.03-1.12])
 Late survival (RR [95% CI] = 1.05 [1.01-1.09])

BIAS

- No publication bias
- No small study bias
- Risk of bias = subjective
- Domains ranged from low (deviation from intended intervention) to serious (confounding)
- Overall = moderate

eTable 4. Risk of Bias in Non-Randomised Studies- of Interventions (ROBINS-I): review authors' judgements about each risk of bias item

Author	D1	D2	D3	D4	D5	D6	D7	Overall
Anand et al. (2021)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Andrade et al. (2022)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Aoki et al. (2023)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Barmparas et al. (2022)	Serious	Moderate	Low	Low	NI	Low	Moderate	Moderate
Bohan et al. (2021)	Moderate	Moderate	Moderate	Low	NI	Low	Moderate	Moderate
Braverman et al. (2021)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Brill et al. (2022)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Duchesne et al. (2021)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Gaines et al. (2021)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Gallaher et al. (2020)	Serious	Moderate	Low	Low	NI	Low	Moderate	Moderate
Gerard et al. (2023)	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Hanna et al. (2020)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Hazelton et al. (2019)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Hazelton et al. (2022)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Lee et al. (2022)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
McLoughlin et al. (2023)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Niemann et al. (2022)	Serious	Moderate	Low	Low	NI	Low	Moderate	Moderate
Perea et al. (2023)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate
Seheult et al. (2018)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Shea et al. (2023)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Siletz et al (2021)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Sperry et al. (2023)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Torres et al. (2023)	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Williams et al (2020)	Moderate	Moderate	Low	Low	NI	Low	Moderate	Moderate

NI: no information

Domain 1: Bias due to confounding; Domain 2: Bias due to selection of participants; Domain 3: Bias in classification of interventions; Domain 4: Bias due to deviations from intended interventions; Domain 5: Bias due to missing data; Domain 6: Bias in measurement of outcomes; Domain 7: Bias in selection of reported result

SENSITIVITY ANALYSES

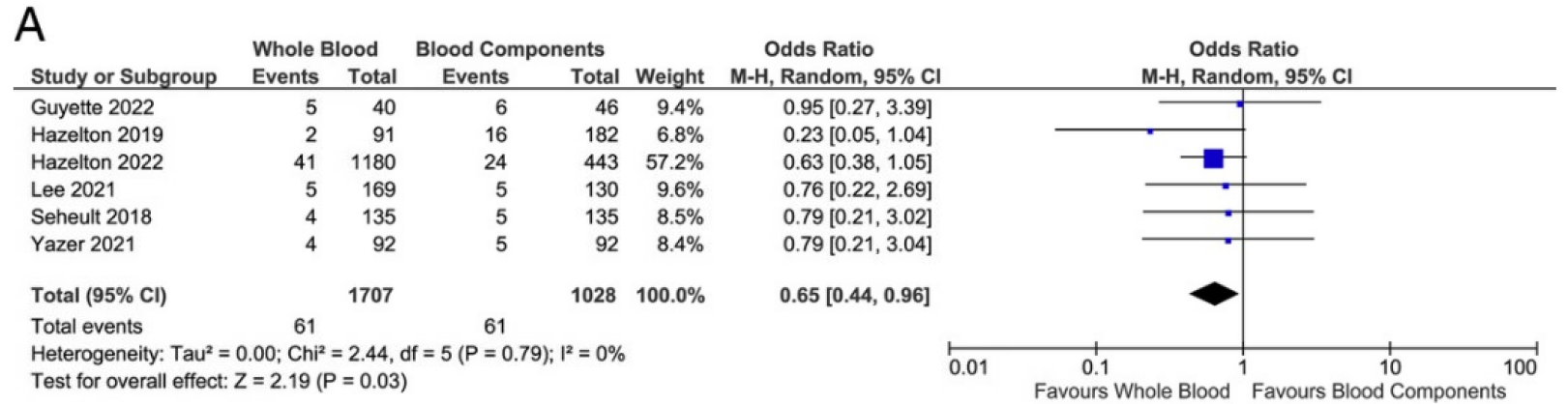
- By analysis type (unadjusted vs adjusted)
 - Early survival – no change in magnitude, direction or significance of outcomes
 - Late survival – no longer significant
- By age group
 - Adult only = early mortality
 - Children only = early and late mortality
- By product type
 - Adding modified LTOWB (n=2), both early and late mortality still significant

VAN DER HORST ET AL, JTACS AUG 2023

- Adults age >15 years
- Through Jan 2023
- Medline, Embase, Cochrane library, CINAHL, Web of science
- Studies conducted in civilian setting (n = 20 total)
- Mortality timepoints:
 - Early (4 hours, 6 hours, and emergency department)
 - 24 hours
 - Late (28 days, 30 days, in-hospital)

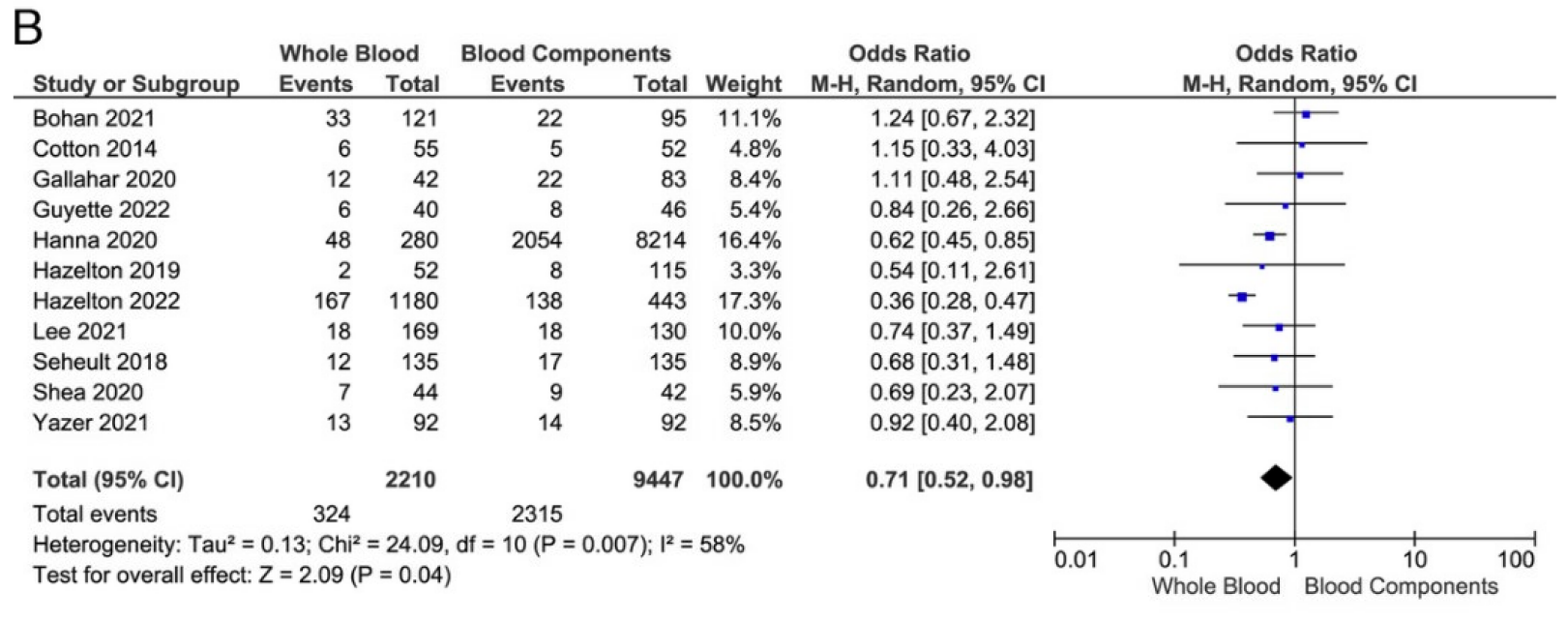
“Early” mortality
(4h, 6h, ED)

N=6 studies



24h mortality

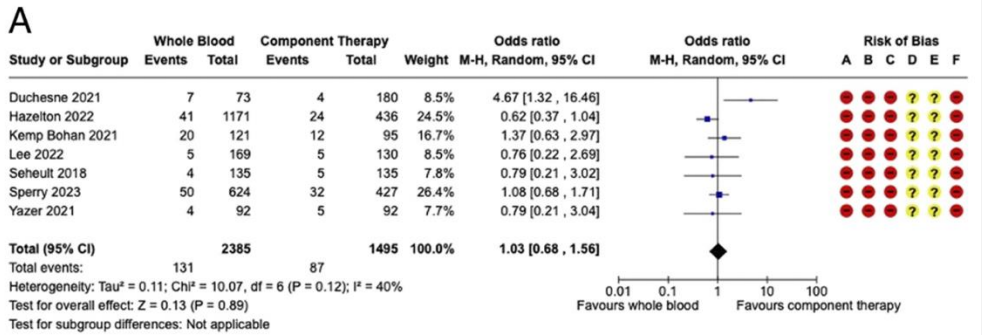
N=11 studies



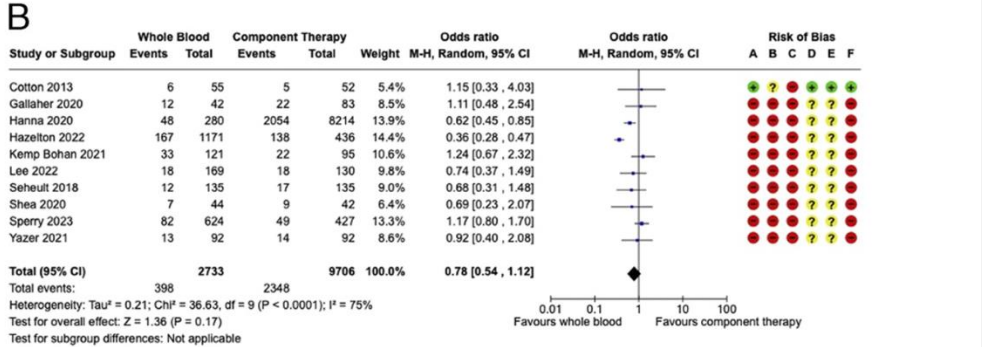
MEIZOSO ET AL JTACS

- Adults age > 15 years
- Through May 2023
- Excluded military and pediatrics
- Medline, Embase, Cochrane CENTRAL, CINAHL Plus, and Web of Science
- Included 21 studies total
- Mortality timepoints = “early”, 24-hour, “late” and “in-hospital”
- Included LR without platelet-sparing filter and “modified” WB with supplemented room temperature platelets
- Secondary outcome: blood product transfusion volume, ICU length of stay, infectious complications

MORTALITY



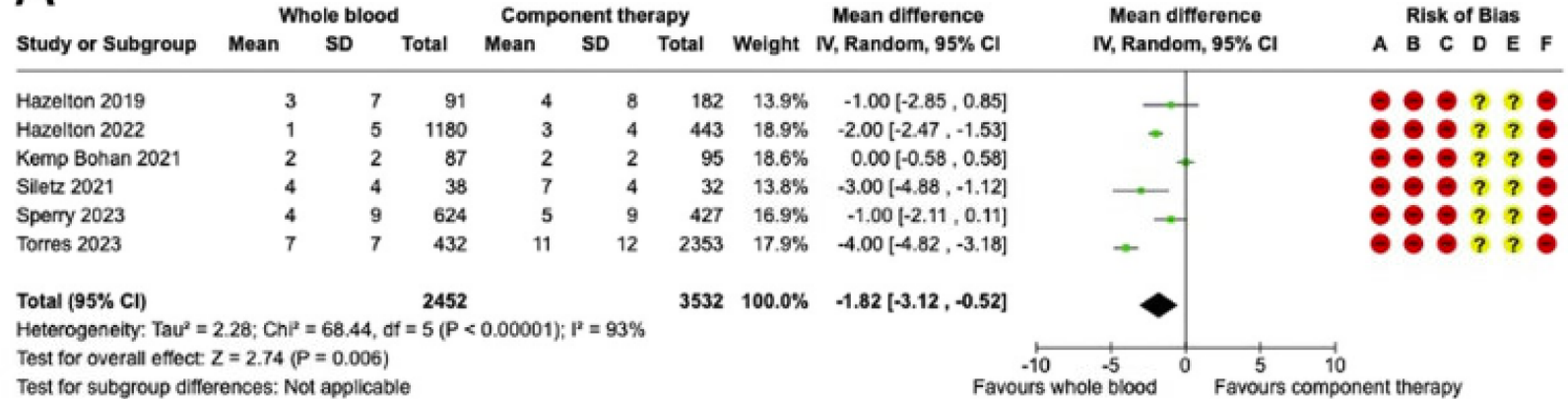
Risk of bias legend
 (A) Random sequence generation (selection bias)
 (B) Allocation concealment (selection bias)
 (C) Blinding of participants and personnel (performance bias)
 (D) Incomplete outcome data (attrition bias)
 (E) Selective reporting (reporting bias)
 (F) Other bias



- N=7 studies (Early)
- N=10 studies (24-hour)
- N=8 studies (Late)
- N=10 studies (In-hospital)

Reduced 4-hour and 24-hour RBC transfusion volume

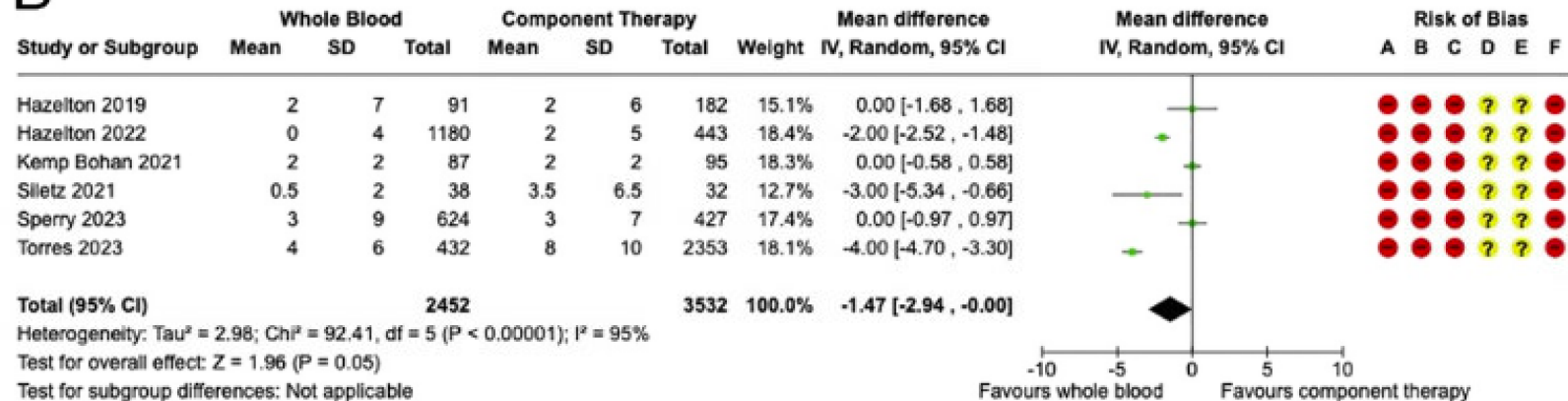
A



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Incomplete outcome data (attrition bias)
- (E) Selective reporting (reporting bias)
- (F) Other bias

B



Reduced 4-hour plasma transfusion volume

PRACTICE MANAGEMENT GUIDELINE FROM THE EASTERN ASSOCIATION FOR THE SURGERY OF TRAUMA

“Seven authors (64%) voted for a conditional recommendation, and four authors (36%) voted that they could not recommend for or against. Thus, we conditionally recommend using WB in adult civilian trauma patients receiving blood transfusions, recognizing that data are limited for certain populations, including women of childbearing age, and therefore, this guideline may not apply to these populations.”

“[LTOWB] should be considered in any bleeding adult male or postmenopausal female patient who presents to a trauma center where WB is immediately available.”

WOMEN

- *“The potential risk of fetal harm in women of childbearing age is a particular concern related to WB transfusion and was considered when formulating the recommendations. However, several studies evaluating the preferences of women regarding emergency lifesaving transfusions, even when there is a small potential risk of fetal harm, have reported that most women would accept this risk.”*

Emergency Transfusion in Females with Childbearing Potential: Mitigating the Risks of Hemolytic Disease of the Fetus and Newborn

November 19-20, 2024 | Hyatt Regency Bethesda



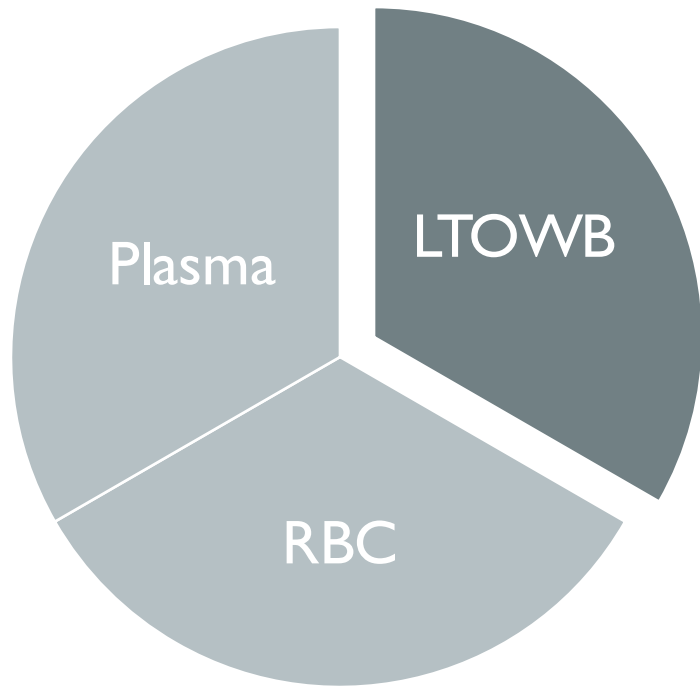


DONOR EXPOSURES

MCLOUGHLIN ET AL JTACS 2023

- TQIP database 2017-2019
- Age >12 years, transfusion within 4 hours
- 390 patients (109 LTOWB, 281 CT)
- Lower total product volumes
- LTOWB cohort → fewer blood product units (~donor exposures)





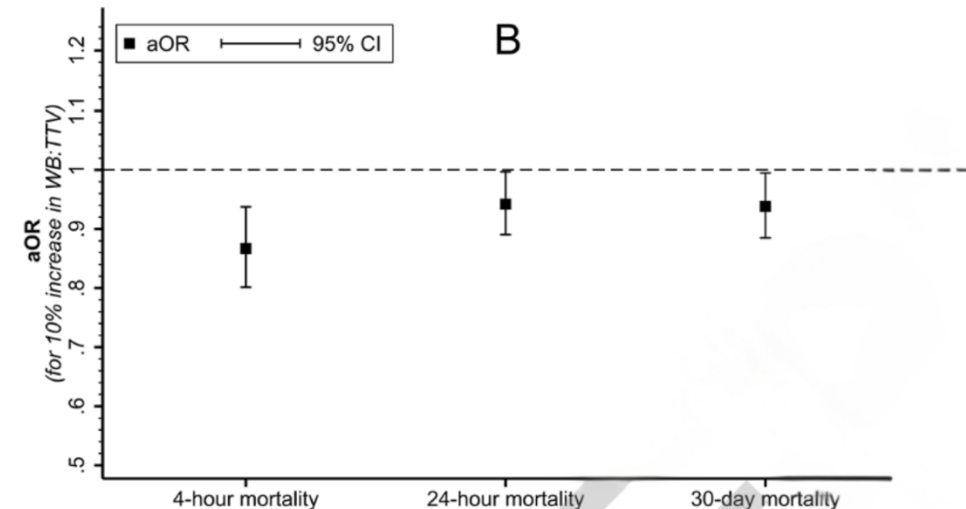
DOSE EFFECT

Whole Blood / Total Transfusion Volume
WB/TTV Ratio

DORKEN-GALLASTEGI ET AL, ANN SURG MAY 2024

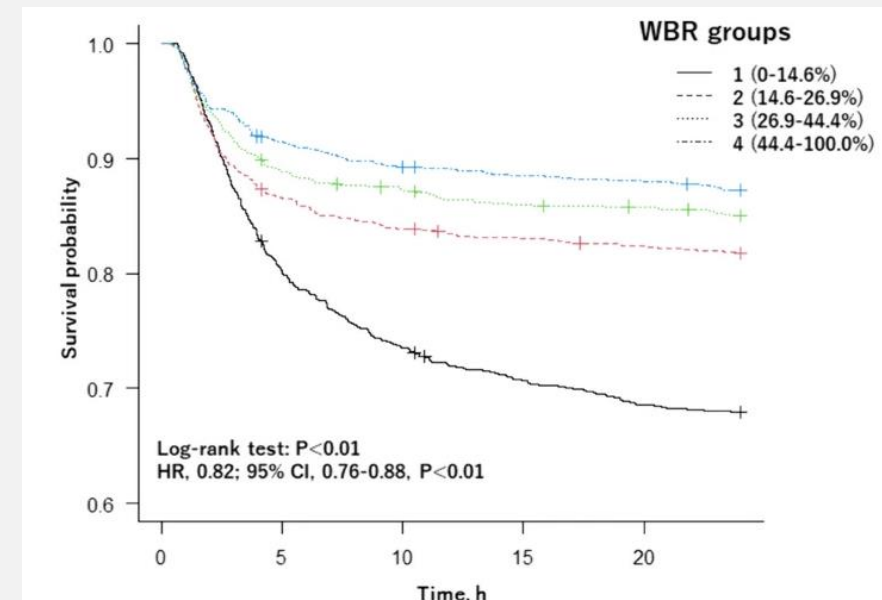
- TQIP database (2020-2021)
- Adults with shock index >1 who received ≥ 4 combined units of red blood cells (RBC) or WB within 4 hours of arrival
- 12,275 patients were included (WB: 2,884 vs. component-only: 9,391)
- Higher WB:TTV ratios were significantly associated with lower 4-hour, 24-hour, and 30-day mortality

- 13% decrease in odds of 4-hour mortality for each 10% increase in the WB:TTV ratio



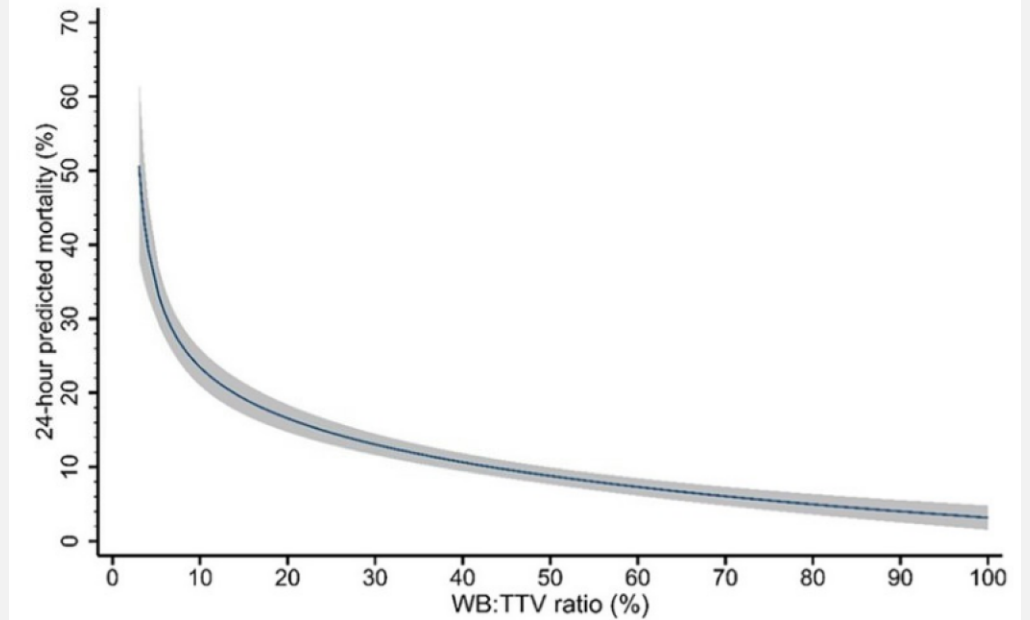
AOKI ET AL, CRIT CARE JUL 2024

- ACS-TQIP (2020 - 2021)
- 4087 adults received WB within 4h of arrival
- Categorized into four groups based on the quartiles of WB:TTV ratio
- Primary outcome: 24-h mortality
- WB units transfused = 2 (2-4)
- The highest WBR quartile had lower
 - 24-h mortality (AOR 0.61, 95% CI 0.46-0.81)
 - 30-day mortality (AOR 0.58; 95% CI 0.45-0.75)



CAMPWALA ET AL JTACS SEP 2024

- ACS-TQIP database 2020-2021
- 4323 children (age <18 years) who received any blood transfusion within 4 hours of hospital arrival
- Calculated WB/TTV ratio
- Any WB transfusion was associated with:
 - 42% decreased odds 4 h mortal (aOR = 0.58 [0.35–0.97]; $p = 0.038$)
 - 54% decreased odds 24h mortal (aOR, 0.46 [0.33–0.66]; $p < 0.001$)
- Each 10% increase in WB/TTV ratio was associated with a 9% decrease in 24-hour mortality



Fractional polynomial model for the relationship between WB/TTV and the estimated probability of 24-hour mortality. Gray area represents 95% CI for the fractional polynomial model.

DOSE
RESPONSE

WHOLE BLOOD:TOTAL BLOOD PRODUCT RATIO IMPACTS SURVIVAL IN INJURED CHILDREN

Single-center observational
study

Pediatric recipients of low
titer group O whole blood

Calculated ratio:
 $\frac{\text{Whole Blood}}{\text{Total Transfusion Volume}}$

95 severely injured
children



LTOWB comprised
59% (33/100) of total
blood product resuscitation

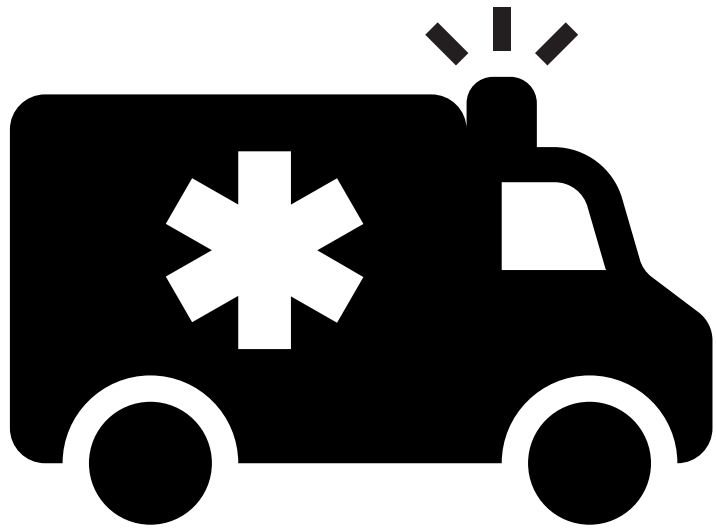
Adjusted for age, sex, mechanism
of injury, injury severity score,
shock index, and GCS score

Higher WB:TTV
ratio independently associated with
increased survival

38% decrease in-hospital mortality
for each 10% increase in the
proportion of LTOWB ($p < 0.001$)

LAMMERS ET AL TSACO APR 2024

- Retrospective review, single center (2019-2022)
- 390 subjects who received 3+ units within 1 hour of arrival
- WB to packed red blood cell ratios (WB:RBC)
- Decreased 4-hour mortality in patients with a WB:RBC \geq 1 at
 - 1 hour (5.9% vs. 12.3%; OR 0.17, p=0.015)
 - 2 hours (5.5% vs. 13%; OR 0.16, p=0.019)
 - 3 hours (5.5% vs. 13%, OR 0.18, p<0.01)
- Decreased 24-hour mortality with a WB:RBC \geq 1 at 24 hours (7.9% vs. 14.6%, p=0.01)
- Decreased 24-hour transfusion requirements with a WB:RBC \geq 1 (12 vs. 24 units, p<0.01)

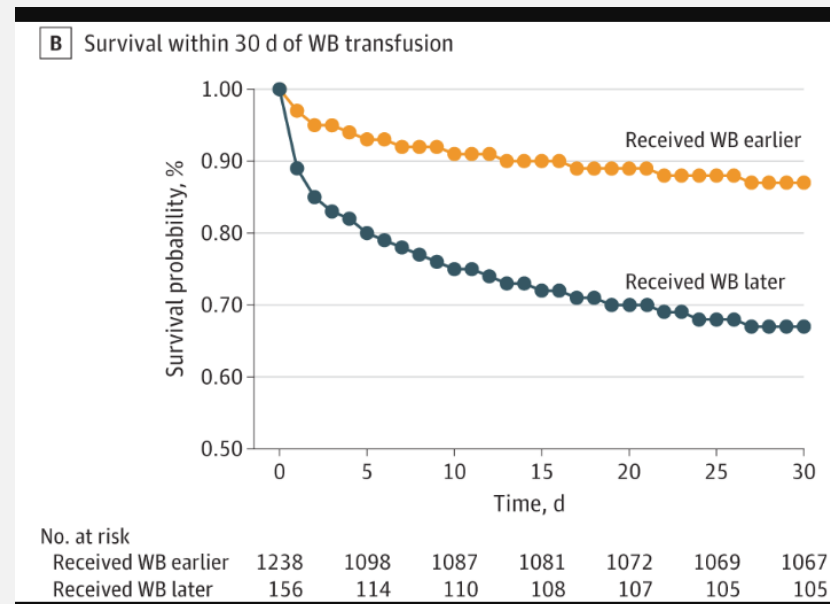


TIMING

TORRES ET AL JAMA SURG APR 2024

Does timing of LTOWB impact survival?

- ACS TQIP 2019-2020
- 1394 patients → Adults in shock who received WB as an adjunct to MTP within 24h of arrival
- When was WB given during the MTP?
→ Early vs Later



Results

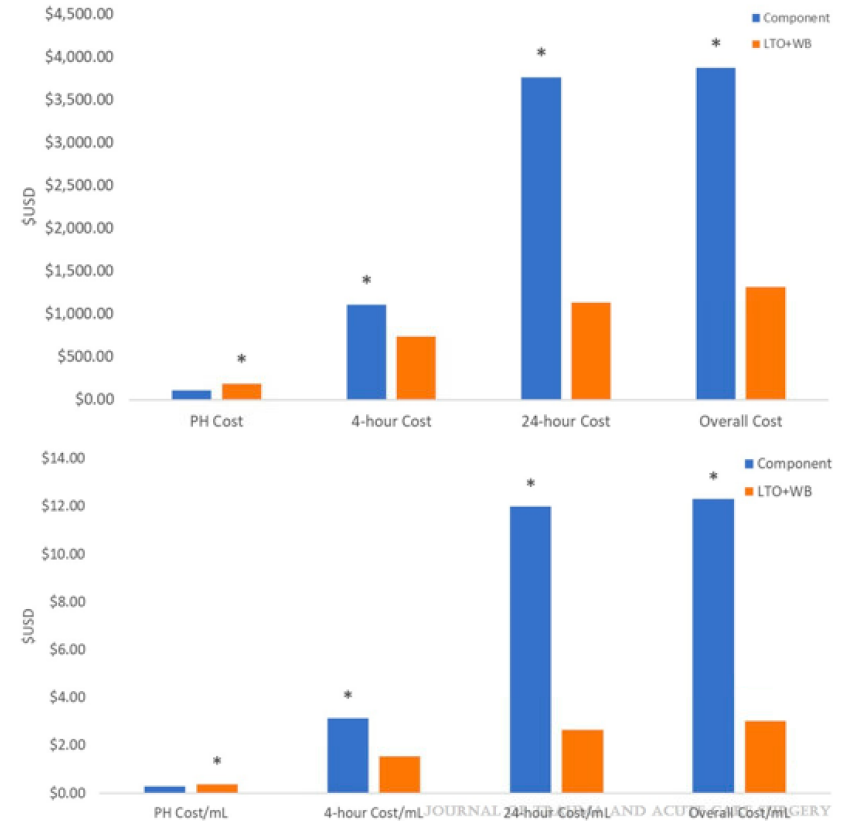
- Every 1-minute increase in the time to initial WB transfusion during the first 4 hours = ↑ mortality
- Most prominent inflection point for reduced survival = **14 minutes** from ED arrival
- Whole blood given earlier vs later at each time point was associated with improved survival



COST

CIARAGLIA ET AL JTACS JUL 2023

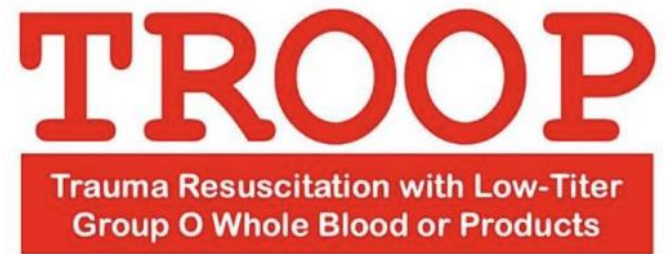
- Pre-post implementation of LTOWB
- Significantly lower mean cost/patient AND cost/patient/mL at 4 hours, 24 hours and overall
- Net decrease in average annual spending of more than \$927,000 due to decrease in mean annual costs associated with CT
- Does not include storage, processing and lab costs



LOOKING AHEAD



Type O Whole blood and assessment of Age early Resuscitation trial



An aerial photograph of Pittsburgh, Pennsylvania, showing the city skyline, the Allegheny River, and several yellow arch bridges. In the foreground, a red trolley with yellow trim is visible on a track, partially obscured by a white-bordered box containing the text "THANK YOU".

THANK YOU