

*THE FUTURE OF WHOLE BLOOD*

# USES FOR WHOLE BLOOD IN PEDIATRICS AND NON-TRAUMA CASES

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NATIONAL  
WHOLE BLOOD  
SUMMIT



University of  
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UPMC | **CHILDREN'S**  
HOSPITAL OF PITTSBURGH

# PEDIATRIC TRAUMA

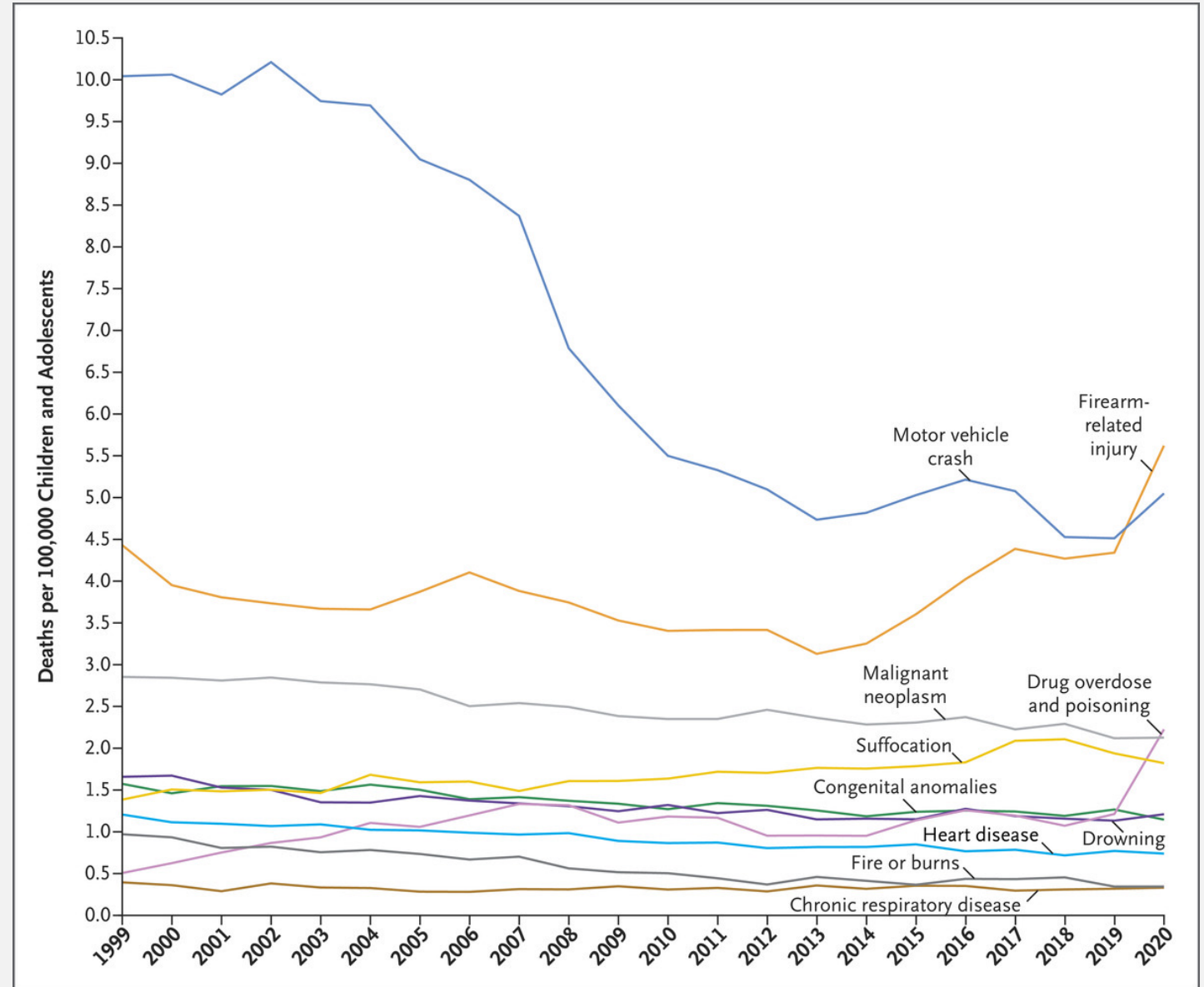
## OUTCOMES FOR CHILDREN WITH MAJOR HEMORRHAGE

- Bleeding is the leading cause of preventable death in children
- 2000 preventable deaths annually in the US due to traumatic bleeding
- 28-day mortality rates in injured children with life threatening hemorrhage (36-50%) are approximately twice that of adults (21-24%)

1. Kwon AM. Eur J Trauma Emerg Surg. 2014;40(3):279-85.
2. Davis JS. J Trauma Acute Care Surg. 2014;77(2):213-8.
3. Fox N. Journal of Emergency Medicine & Critical Care. 2018;4(1):4.
4. Leonard JC. 2021;49(11):1943-54.
5. Holcomb JB. JAMA Surg. 2013;148(2):127-36.
6. Holcomb JB. Jama. 2015;313(5):471-82.

# UNDERSTANDING PEDIATRIC TRAUMA IS AN URGENT PRIORITY

Leading Causes of Death among  
Children and Adolescents in the  
United States, 1999 through 2020.  
JE Goldstick et al. N Engl J Med  
2022;386:1955-1956.

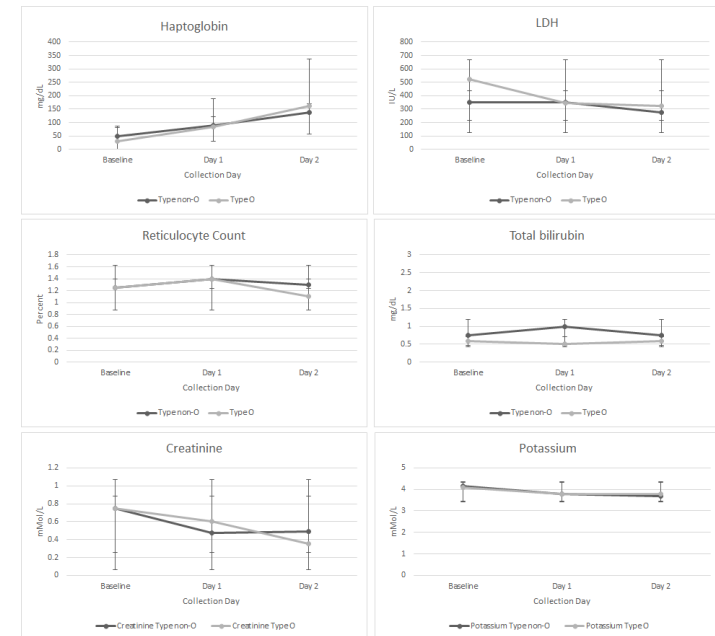


## LTOWB IN CHILDREN: 2016 - PRESENT

- Increasing number of centers in the US use LTOWB for injured children
  - At least 15 pediatric trauma centers have a LTOWB program
  - Plus adult centers that use LTOWB for adolescents
- More with programs in development or with interest
- Increasing data in children that show:
  - Feasibility
  - Safety
  - Efficiency
  - Effectiveness

# SAFETY

- No major transfusion reactions
- No increase in organ failure
- No increase in hospital complications
  - AKI
  - Sepsis
  - ARDS
  - Thromboembolism
- No increase in hemolysis



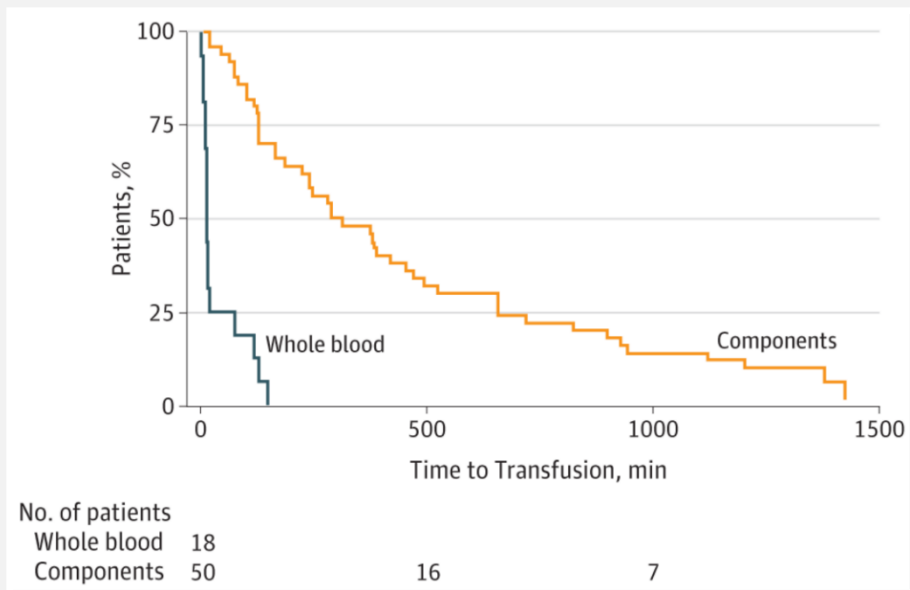
# SAFETY

- Across a Range of Product Characteristics
  - Rh positive and negative
  - Leukocyte reduced and Non Leukocyte reduced
  - Titer <1:50 - < 1:200
- Vulnerable populations
  - Youngest age
  - Weight < 20kg

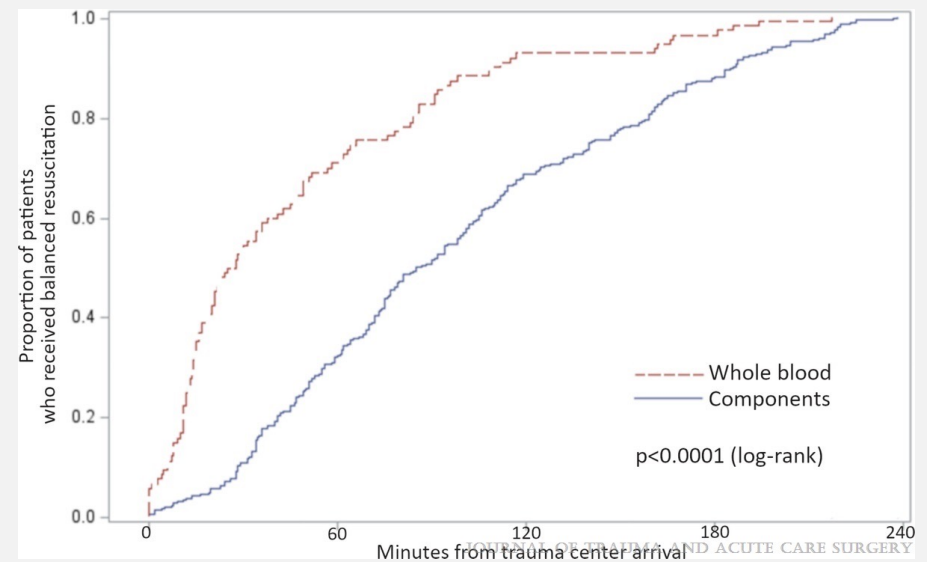
**TABLE 4.** Comparison of Laboratory Indicators of Hemolysis Among the Two Groups

	LTOWB, n = 73	COMP, n = 91	<i>p</i>
24-h Creatinine	0.97 (0.82, 1.21)	0.76 (0.57, 1.01)	<0.001
24-h Potassium	3.9 (3.7, 4.2)	3.9 (3.6, 4.2)	0.628
24-h Total bilirubin	0.8 (0.5, 1.3)	0.6 (0.4, 1.0)	0.227
24-hr LDH	405 (304, 773)	436 (360, 669)	0.924
24-h Haptoglobin	56 (36, 64)	27 (12, 62)	0.276
24-h PaO <sub>2</sub> /FIO <sub>2</sub>	390 (260, 490)	397 (217, 526)	0.526
48-h Creatinine	0.76 (0.64, 1.02)	0.62 (0.38, 0.87)	0.016
48-h Potassium	3.8 (3.6, 4.2)	3.9 (3.6, 4.2)	0.785
48-h Total bilirubin	0.9 (0.6, 1.4)	0.9 (0.6, 1.3)	0.977
48-h LDH	385 (311, 586)	355 (314, 436)	0.483
48-h Haptoglobin	67 (58, 83)	93 (62, 167)	0.394
48-h PaO <sub>2</sub> /FIO <sub>2</sub>	359 (247, 472)	382 (320, 465)	0.158
72-h Creatinine	0.65 (0.54, 0.94)	0.58 (0.37, 0.83)	0.122
72-h Potassium	3.9 (3.6, 4.1)	3.8 (3.6, 4.0)	0.441
72-h Total bilirubin	0.9 (0.6, 1.7)	0.6 (0.4, 1.3)	0.180
72-h LDH	321 (217, 447)	408 (234, 570)	0.530
72-h Haptoglobin	124 (52, 191)	103 (81, 116)	0.867
72-h PaO <sub>2</sub> /FIO <sub>2</sub>	356 (258, 420)	355 (277, 477)	0.463

# EFFICIENCY



Leeper et al JAMA Pediatrics 2018



McLoughlin et al JTACS 2024



# MITIGATING SHOCK AND COAGULOPATHY

Figure 2 -

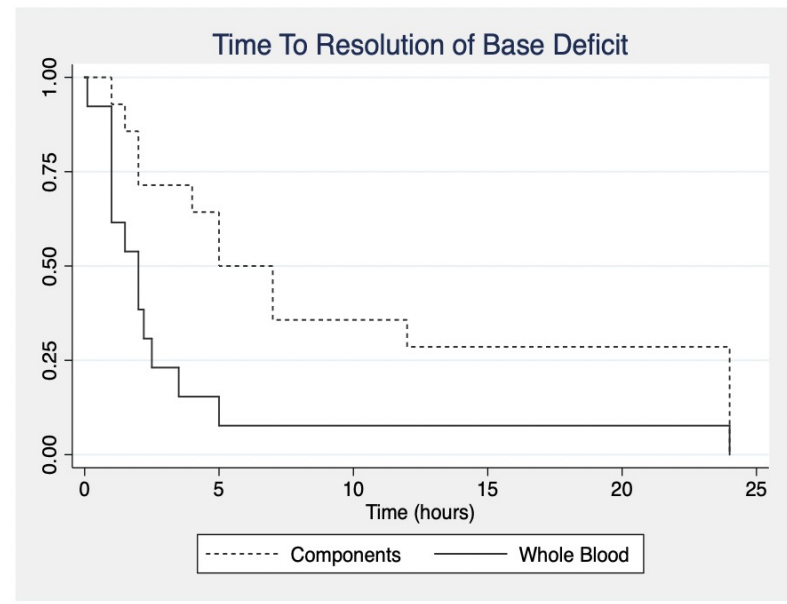
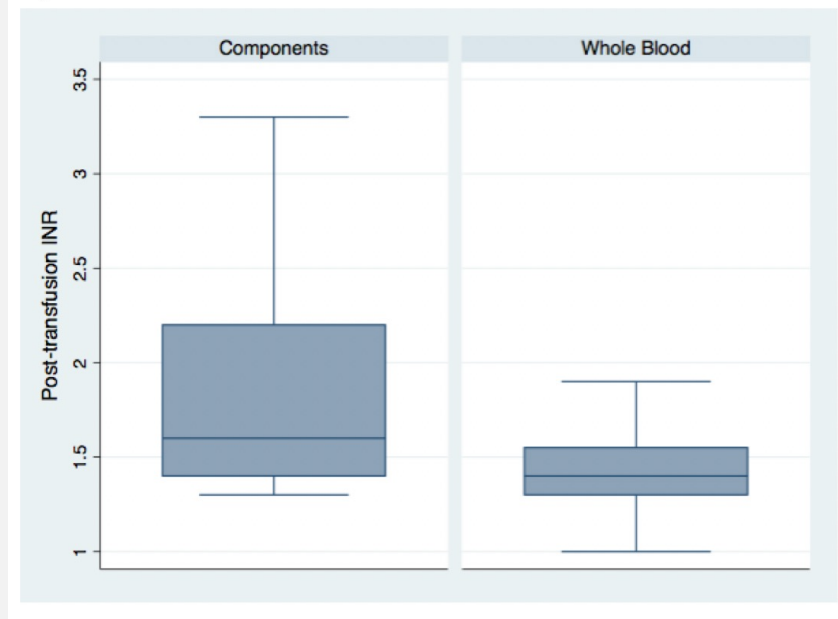


Figure 3



# PRODUCT TRANSFUSION VOLUME

- TQIP database
- In LTOWB group as compared to CT group:
  - Less plasma and platelet
  - Less volume overall

TABLE 2. Transfusion Requirements

	CT (n = 270)	WB-CT (n = 135)
4-h Transfusions, median (IQR), mL/kg		
PRBC	31 (22–57)	19 (11–31)
Plasma	12 (9–31)	9 (0–21)
Platelets	4 (4–10)	0 (0–6)
WB	—	13 (9–20)
Total blood products	48 (33–95)	35 (22–73)
24-h Transfusions, median (IQR), mL/kg		
PRBC	36 (25–71)	22 (15–53)
Plasma	17 (11–46)	11 (0–25)
Platelets	6 (4–13)	0 (0–9)
WB	—	14 (10–23)
Total blood products	53 (36–119)	39 (24–97)

\*Statistically significant.

IQR, interquartile range; PRBC, packed red blood cell.

## PRODUCT VOLUME & DONOR EXPOSURE

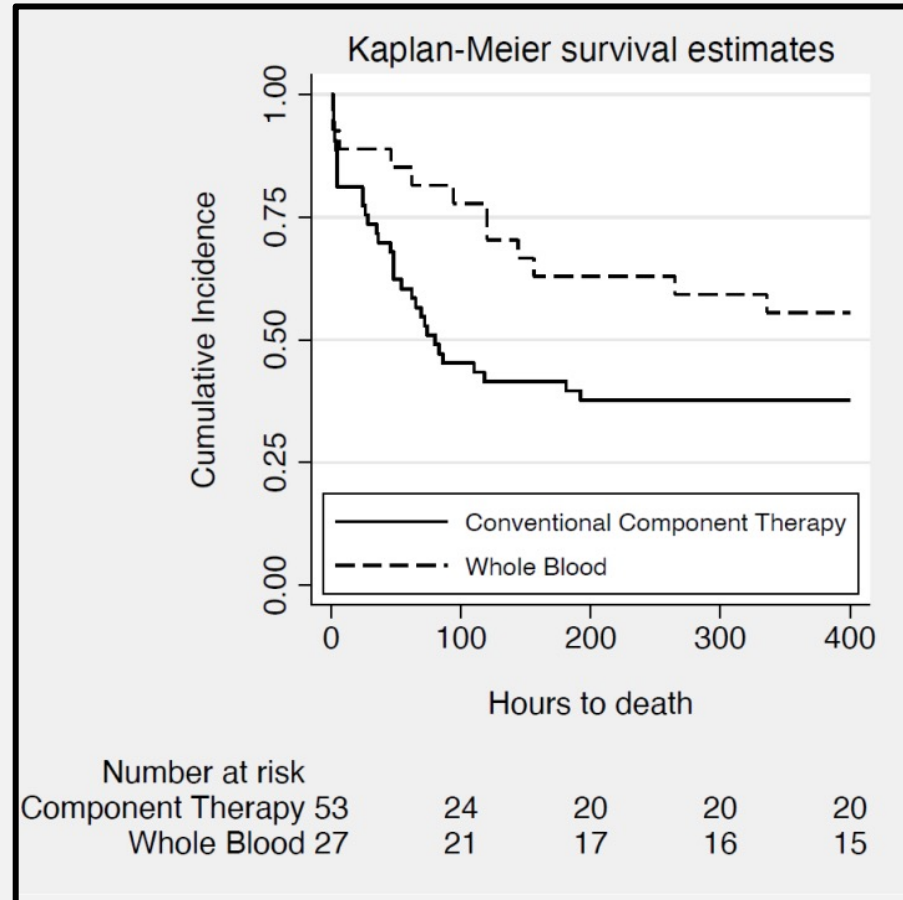
<i>Transfusion details &amp; outcomes</i>				
Time to balanced resuscitation, minutes	72 (34-119)	87 (50-141)	28 (13-66)	<0.0001
Number of transfusion exposures in first four hours	3.70 (2.05)	3.89 (1.79)	3.21 (2.54)	0.01
Total transfused blood product volume in first four hours, mL/kg	75 (39-131)	85 (46-126)	50 (20-133)	0.01

- 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)

# SURVIVAL

Children receiving massive transfusion:

- 72 hours (AOR 0.23;  $p=0.009$ )
- 28 days (AOR 0.41;  $P$  0.02)



## SURVIVAL

- 76 LTOWB vs 91 CT
- Median age 14, ISS 26
- After adjusting for inverse probability of treatment weights, LTOWB was associated with improved survival

**TABLE 6.** Inverse Probability Weighted Analysis for 30-d Survival

	OR	95% CI	<i>p</i>
Whole blood group	2.48	1.16–5.47	0.02
Age, per year	1.004	1.0001–1.0006	0.003
Male sex	0.46	0.20–1.04	0.07
ISS, per point	0.93	0.89–0.96	<0.001
Scene SBP, per mm Hg	1.00	0.99–1.01	0.93
Arrival lactate, per mmol/L	0.76	0.67–0.84	<0.001

# SURVIVAL

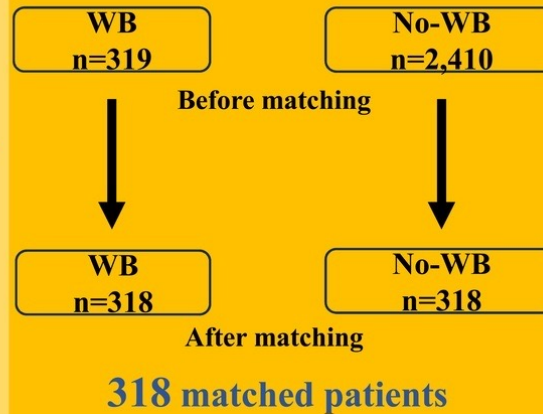
## Association Between Whole Blood Transfusion and Mortality Among Injured Pediatric Patients

### STUDY DESIGN

- ACS-TQIP 2020-2021
- Injured children (age ≤ 16 yrs)
- Blood transfusion < 4 hrs of hospital arrival



### PATIENT STRATIFICATION



### OUTCOMES

#### 24-hour mortality

WB (7.3%) vs No-WB (12.7%),  $p=0.033$

#### 30-day mortality

WB (19.5%) vs No-WB (27.0%),  $p=0.031$

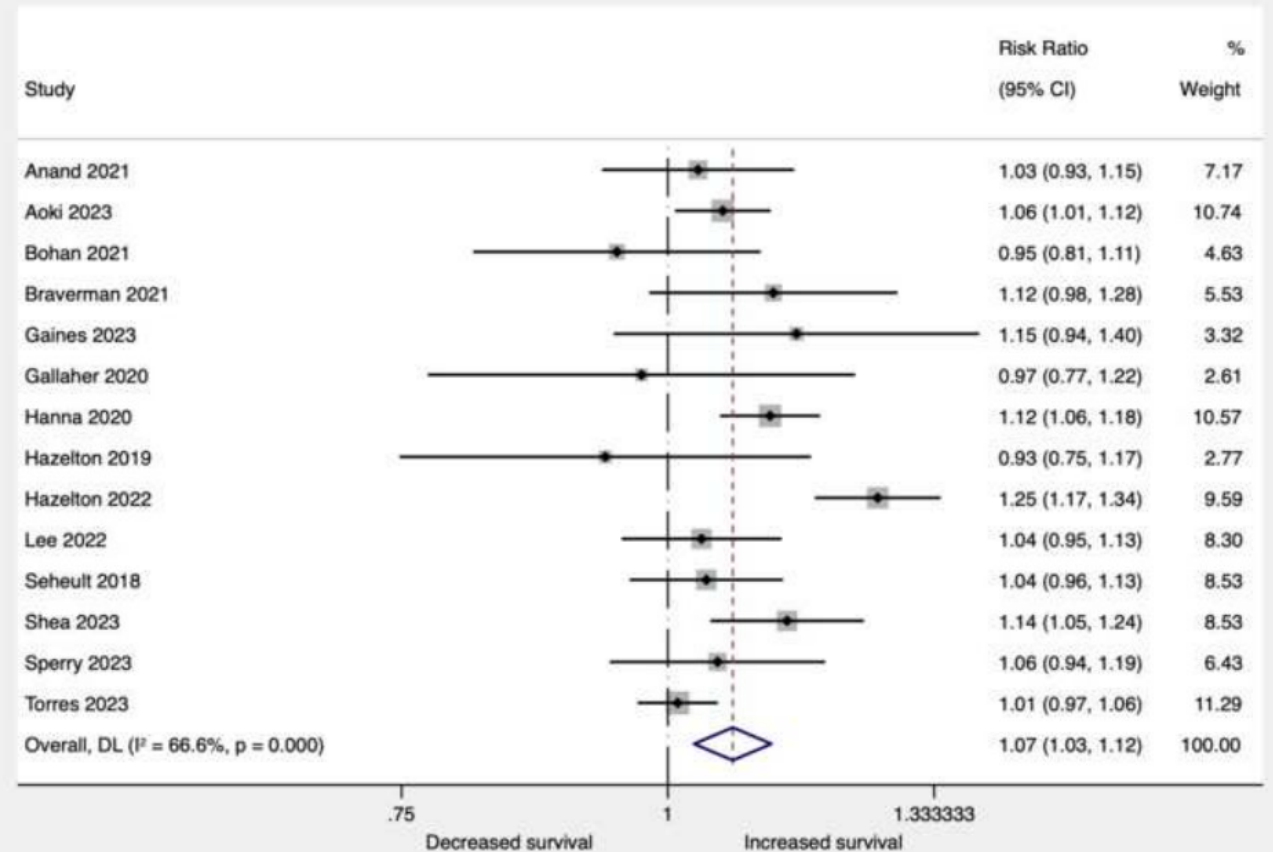


#### WB transfusion

Improved mortality among pediatric patients requiring blood transfusion < 4 hours of arrival

# SURVIVAL

- Meta-analysis
- Combines pediatric/adolescent/adult cohorts
- 14 studies reported early mortality and 22 studies reported late mortality
- 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])



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:  
Whole Blood  
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 ( $p < 0.001$ )



## BARRIERS

- Availability: robust blood supply
- Mature system with the means to recycle/offload products near expiration
- Lack of standard guideline, practice variation
- Buy in from pediatric providers
- Concerns about waste, cost, Rh exposure...
- Do the current data support a practice change?

# MATIC-2

## Domains

- 1) Blood product domain = LTOWB vs CT
  - 2) Hemostatic Adjunct domain = TXA vs Placebo
- 20-24 US high volume pediatric trauma centers
  - 1000 children
  - 5-10 years
  - Funded by the Biomedical Advanced Research and Development Authority (BARDA)



ADULT NON-TRAUMA

## LTOWB IN NON-TRAUMATIC BLEEDING ETIOLOGIES

- LTOWB is part of the massive transfusion protocol (MTP) for any patient with life-threatening bleeding at an increasing number of US centers
- Not well studied: few case reports and case series
- Common etiologies: GI, obstetric hemorrhage<sup>1,2</sup>

1. Smith et al, American Surgeon, 2023

2. Nowadly et al, Military Medicine 2022

## LTOWB PROGRAMS FOR OBSTETRIC HEMORRHAGE

- Postpartum hemorrhage has been a leading cause of worldwide maternal death (25%), this rate is increasing
- The International Federation of Gynecology and Obstetrics recommends that whole blood can be used in cases of massive hemorrhage
- LTOWB programs specifically for obstetric hemorrhage have been described: University Hospital in San Antonio, TX and Intermountain Health in Utah



# OBSTETRIC HEMORRHAGE

Obstetric patients transfused with whole blood (n = 25)		
Characteristics	Median	Range
Age (y)	30.8	19–57
Gestational age (wk)	36.5	4–42.4 <sup>a</sup>
Length of hospital stay	4	1–4
Indications	N	%
Uterine atony	8	32
Coagulopathy/DIC	5	20
Accreta/percreta/increta	3	12
Amniotic fluid/pulmonary embolism	3	12
Uterine rupture	2	8
Ruptured ectopic pregnancy <sup>a</sup>	2	8
Outcomes	N	%
ICU admission	19	76
Hysterectomy	4	16
Cardiac arrest	4	16
ECMO support	1	4
Maternal death	2	8
Neonatal death	5	20
Transfusions	Median	Range
Estimated blood loss (mL)	3,250	800–12,000
Units of LTOWB transfused	3	1–8
Age of the LTOWB at transfusion <sup>b</sup>	10	(8–13) IQR
Units of components transfused	7	2–44

Factor	Whole blood (n = 16)	Component (n = 18)	p Value
Admission hemoglobin (g/dl)	10.5 ± 1.5	10.7 ± 1.3	.626 <sup>a</sup>
Operative time (min)	319.6 ± 161.1	230.7 ± 128.5	.08 <sup>a</sup>
Urinary stent placement	13 (81)	11 (61)	.27 <sup>c</sup>
Uterine artery embolization	8 (50)	3 (17)	.076 <sup>c</sup>
EBL (ml)	2600 (2000, 4750)	3000 (1875, 5250)	.90 <sup>b</sup>
Component transfusion			
Whole blood	3.5 (1.3, 4)	–	–
Red blood cells	0 (0, 2)	4.5 (2, 6.8)	.003 <sup>b</sup>
Platelets	0 (0, 0.8)	0 (0, 1)	.89 <sup>b</sup>
Fresh frozen plasma	0 (0, 3.3)	3 (0, 5)	.001 <sup>b</sup>
Cryoprecipitate*	0 (0, 0)	0 (0, 0)	.18 <sup>b</sup>
Volume transfused (ml)**	2607	4683	.03 <sup>a</sup>

Carr et al, American Journal of Perinatology Reports 2024

Munoz et al Journal of Maternal Fetal & Neonatal Medicine 2022

# PEDIATRIC NON-TRAUMA

# PEDIATRIC NON-TRAUMA

## Descriptive cohort of n=16 pediatric recipients of LTOWB during massive transfusion

<b>Age (years)</b>	13 (8-16)
<b>Sex</b>	
Male	8 (50)
Female	8 (50)
<b>Etiology of bleed</b>	
<b><u>Medical</u></b>	4(25)
GI	5(31)
Cardiorespiratory	1(6)
ENT	1(6)
Gyne	
<b><u>Surgical</u></b>	3(19)
Cardiothoracic	1(6)
Vascular	1(6)
Abdominal Transplant	
<b>Clinical outcomes</b>	
Mortality	7(41)
ICU days	4(.25-35)
Hospital days	5 (1.25-47.5)

\*Unpublished data: Feeney et al, in press



## NEONATAL NON- TRAUMA

- Carr et al, American Journal of Perinatology Reports 2024

## Descriptive cohort of n=5 neonatal recipients of LTOWB during massive transfusion

Neonatal patients transfused with whole blood (n = 5)		
Characteristics	Median	Range
Gestational age (wk)	26.3	25.1–36.1
Apgar (5 min)	5	2–8
Lowest pH	6.91	6.64–7.04
Maximum total bilirubin (mg/dL)	7	2.9–9.5
Indications	N	%
Fetomaternal hemorrhage	2	40
TRAP (donor)	1	20
Intestinal perforation/ hemorrhagic shock	1	20
Maternal motor vehicle accident	1	20
Outcomes	N	%
No or grade 1 IVH	3	60
IVH grade 2	1	20
IVH grade 3 or 4	0	0
Diagnosis of HIE (moderate/severe)	1	20
Died (redirection of care)	1	20
Transfusions	Median	Range
Volume of LTOWB transfused (mL/kg)	20	10–40
Age of the LTOWB at transfusion <sup>a</sup>	6	(4.5–8) IQR
Number of components transfused	2	1–6

## **WHOLE BLOOD VERSUS RED CELL CONCENTRATES FOR CHILDREN WITH SEVERE ANAEMIA: A SECONDARY ANALYSIS OF THE TRANSFUSION AND TREATMENT OF AFRICAN CHILDREN (TRACT) TRIAL**

- Inclusion: children admitted to hospital with severe uncomplicated anemia
- n= 3188 children, median age 37 months (IQR 18-64)
- Whole blood was the first pack provided for 1632 (41%) of 3992 transfusions
- Whole blood cohort had higher 8h hemoglobin, less likely to require additional transfusion, and shorter length of stay
- No difference in mortality or readmission

## FUTURE STUDIES



- Identify optimal resuscitation strategy in injured children
- Identify optimal resuscitation strategy in nontraumatic bleeding
- Diverse etiologies of bleeding; different patient phenotype → unique strategy to treat?



THANK YOU