

EPIDEMIOLOGY, OUTCOMES, & GAPS IN KNOWLEDGE FOR TRAUMATIC BLEEDING IN CHILDREN

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PEDIATRIC TRAUMA: EPIDEMIOLOGY

MAGNITUDE OF THE PROBLEM

81,254,355

Population

35,000,000

Pediatric Trauma ED Visits

\$24.9 Billion

ED/Inpatient Trauma Costs

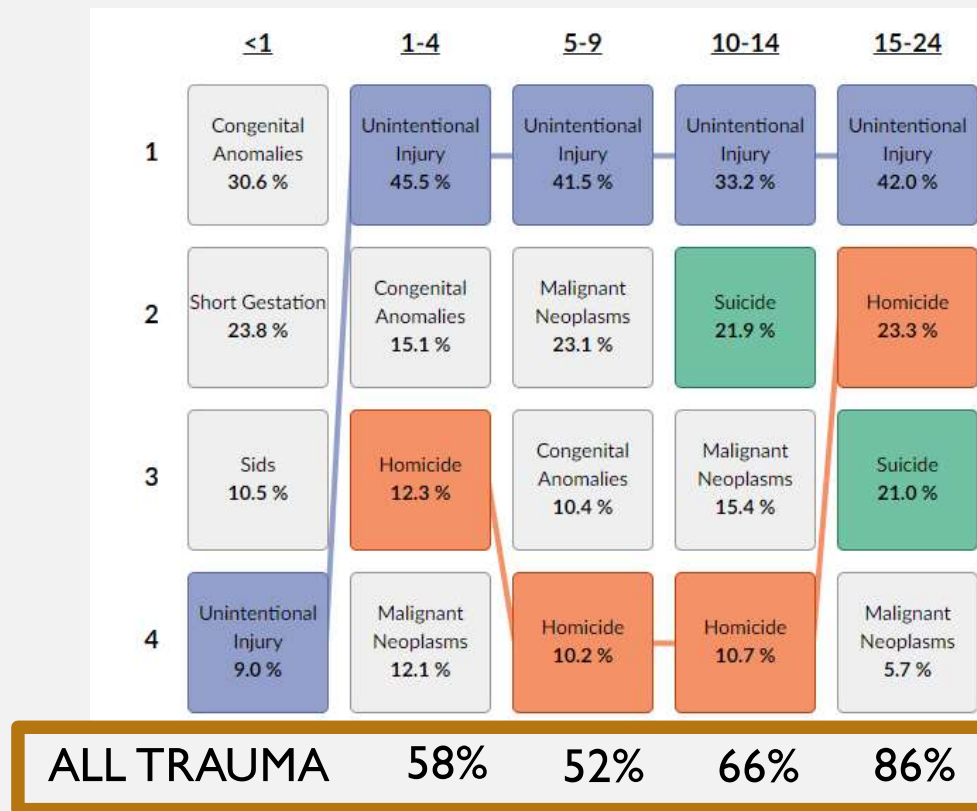
15,447

Number of Deaths

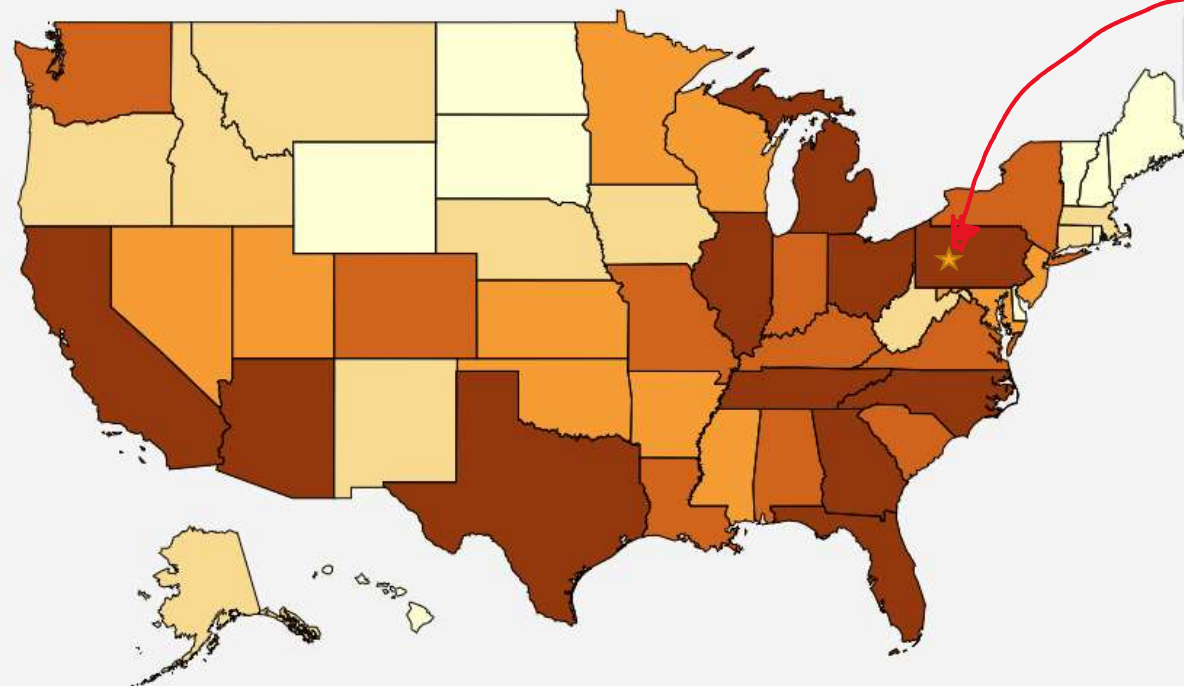
802,563

Years of Potential Life Lost

CAUSES OF DEATH BY AGE GROUP: TRAUMA KILLS CHILDREN IN THE US



GEOGRAPHIC DISTRIBUTION OF INJURY

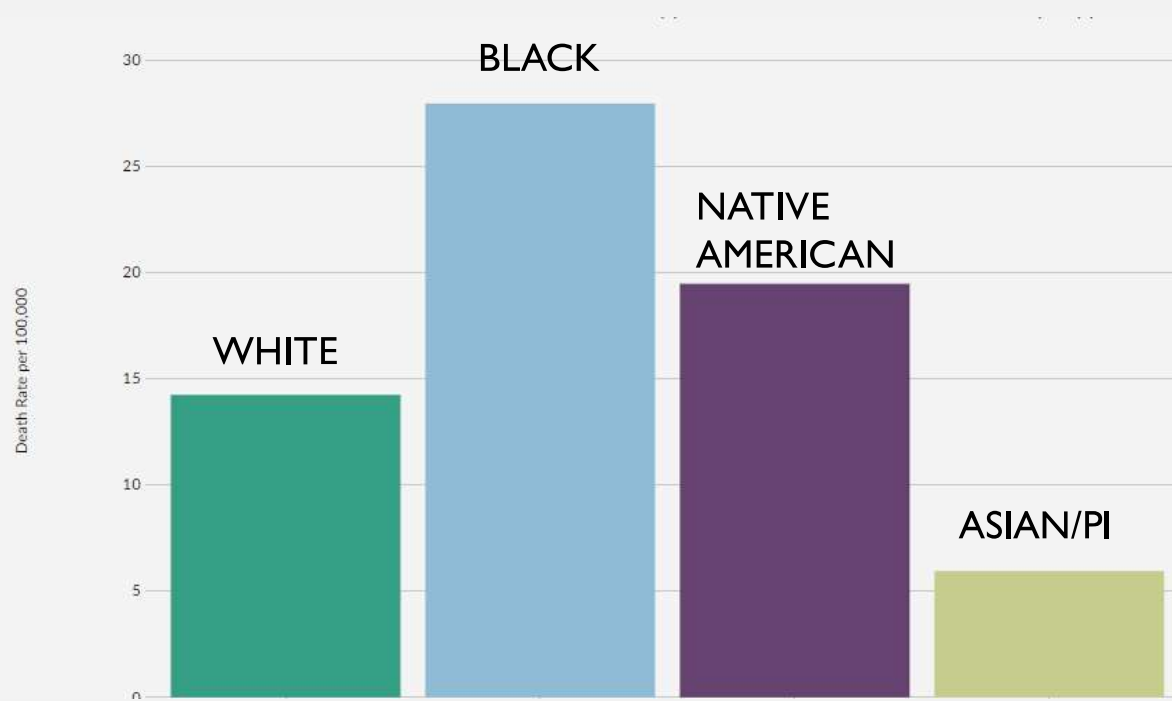


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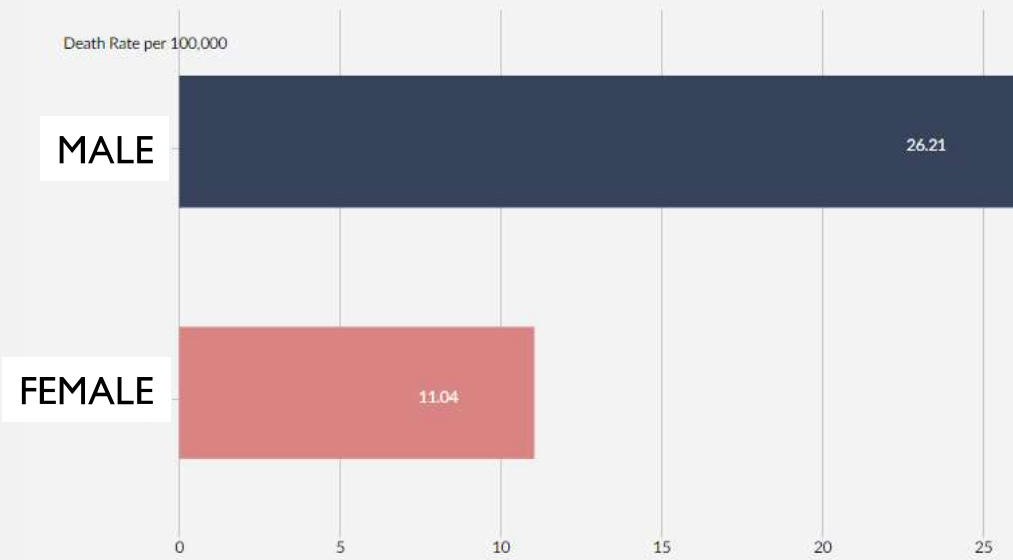
Legend

- 15 to 61
- 61 to 140
- 140 to 237
- 237 to 354
- 354 to 1,285
- Suppressed Value

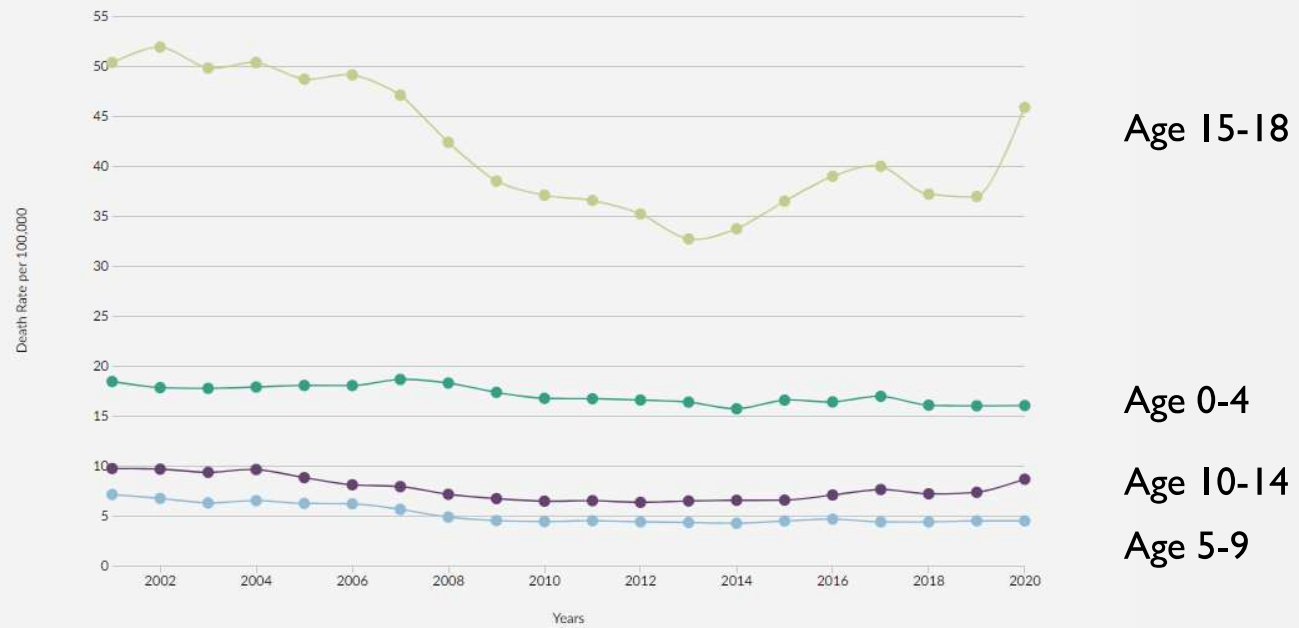
ADJUSTED DEATH RATE BY RACE



DEATH RATE BY SEX

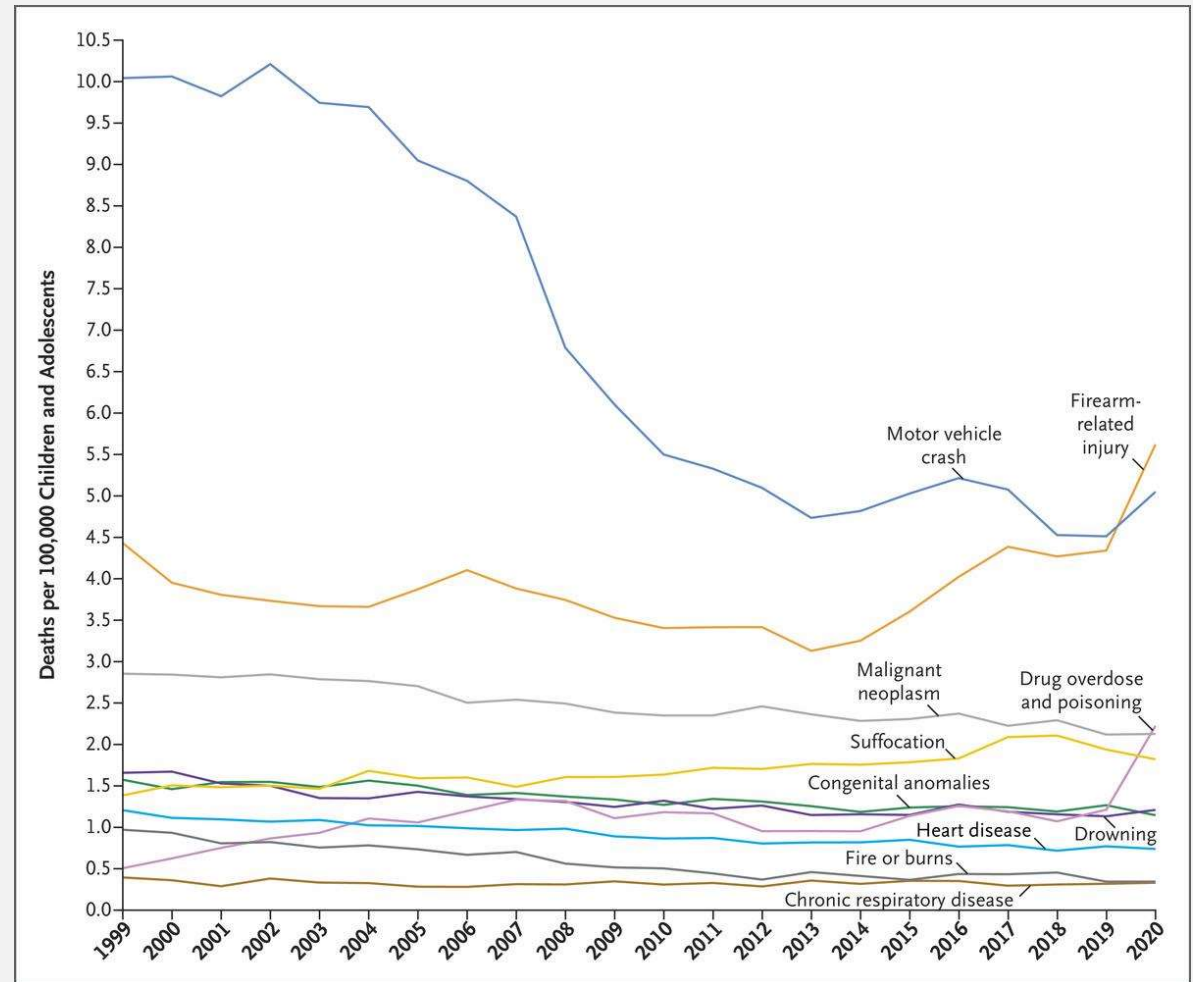


DEATH PER 100,000 BY AGE GROUP



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.



OUTCOMES

MAJOR HEMORRHAGE

- Bleeding is the leading cause of *preventable* death in this population.¹⁻³
 - 2000 preventable pediatric deaths per year in the US due to traumatic bleeding
- 28-day mortality rates in injured children with life threatening hemorrhage (LTH) range from 36-50%⁴
- Approximately at least twice that of injured adults (21-24%)⁵⁻⁶

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.

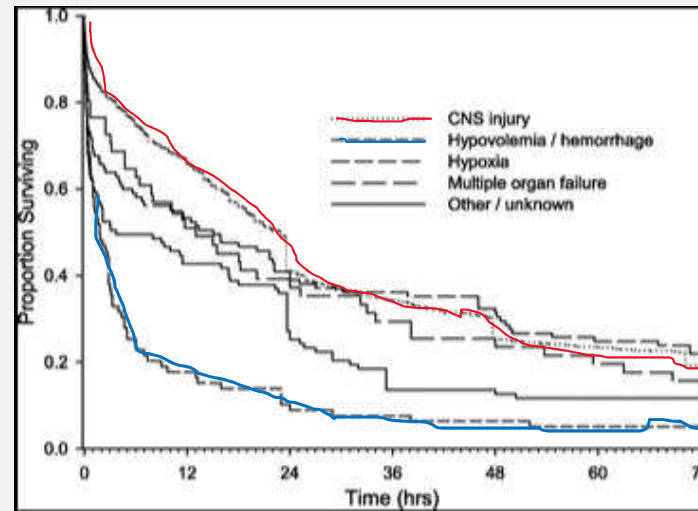
4. Leonard JC. 2021;49(11):1943-54.

5. Holcomb JB. JAMA Surg. 2013;148(2):127-36.

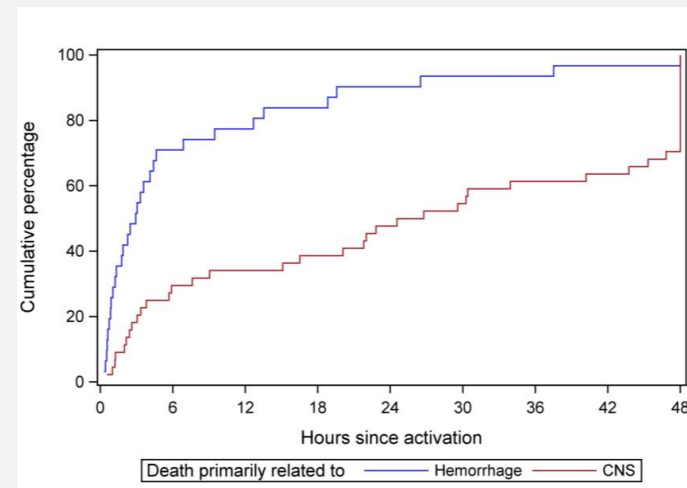
6. Holcomb JB. Jama. 2015;313(5):471-82.

DEATH OCCURS QUICKLY

- Median time to death:
- Hemorrhage = 17 hours
- CNS injury = 52 hours



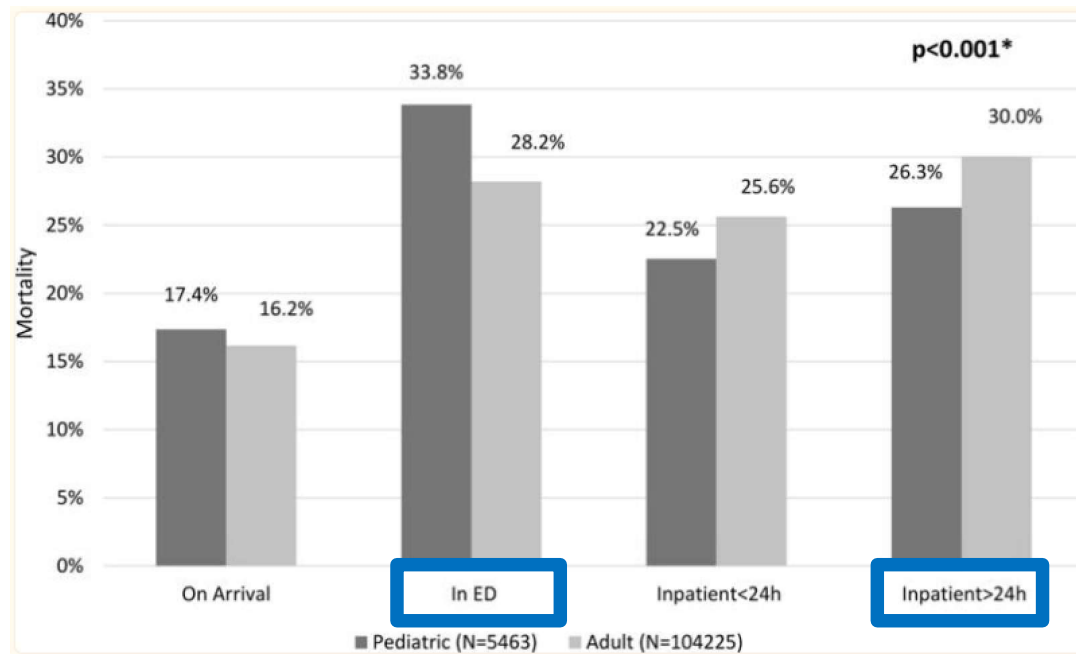
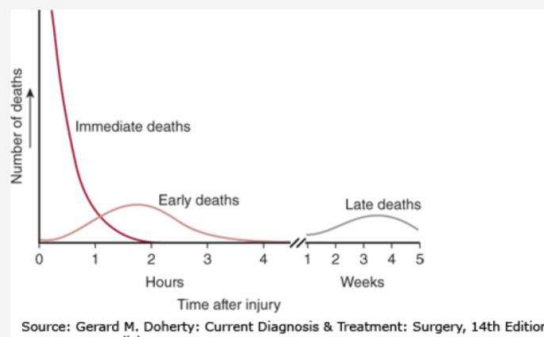
Burd et al JTACS



Leonard et al CCM

EARLY DEATH PREVALENT, LATE DEATH UNCOMMON

- Compared to adults, children have a higher proportion of early death versus late death



McLaughlin et al. Timing of Mortality in Pediatric Trauma Patients: A National Trauma Databank Analysis
J Pediatr Surg. 2018 Feb;53(2): 344–351.

LATE COMPLICATIONS AFTER TRAUMA

Less late death due to:

1. lack of comorbidities
2. lower incidence of MSOF

Complication Prevalence in Late Mortality Pediatric Patients (N=889).

Complication type*	N (%)
Acute Respiratory Distress Syndrome	127 (14.29)
Pneumonia	69 (7.76)
Acute Kidney Failure/Injury	29 (3.26)
DVT/PE	10 (1.12)
Decubitus Ulcer	9 (1.01)
Urinary Tract Infection	6 (0.67)
Sepsis	4 (0.45)
Catheter Associated Bloodstream Infection	1 (0.11)
Pulmonary Thrombosis	1 (0.11)
Deep Space SSI	0 (0)

McLaughlin et al. Timing of Mortality in Pediatric Trauma Patients: A National Trauma Databank Analysis
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GAPS IN KNOWLEDGE

WHAT TREATMENT
STRATEGIES
BENEFIT BLEEDING
CHILDREN



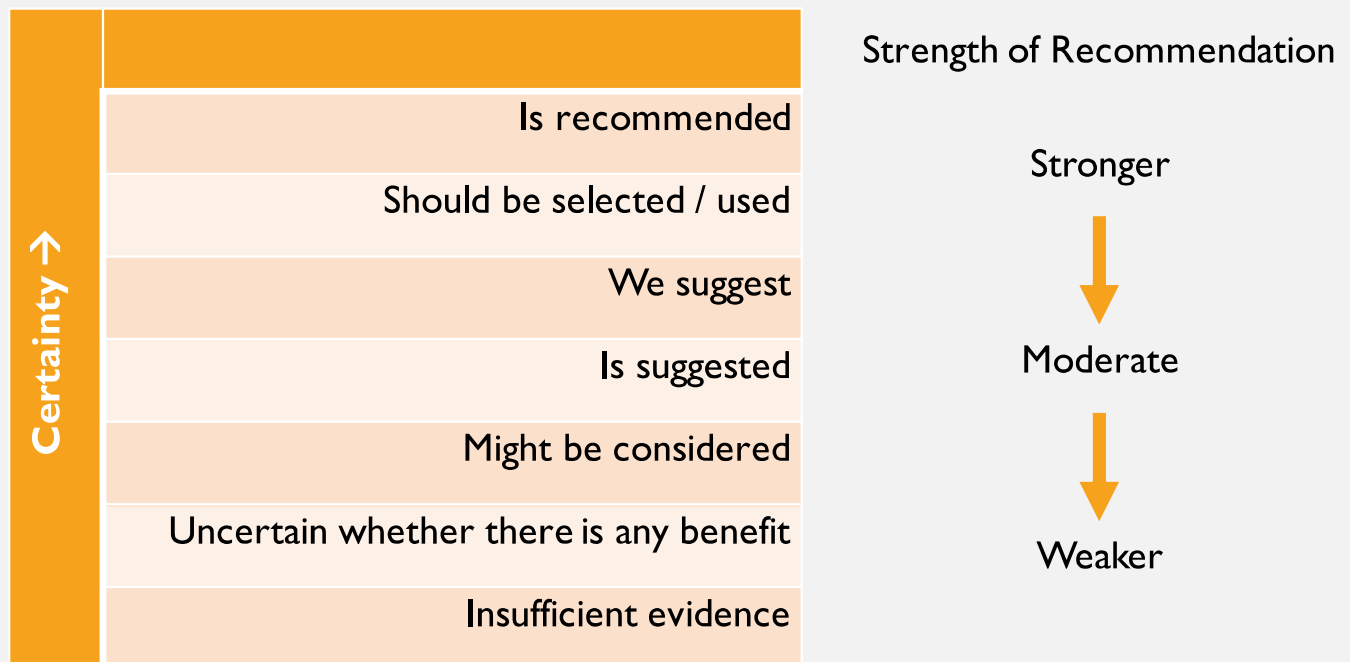
Pediatric Trauma Hemorrhagic Shock Treatment Guideline Consensus Conference



“Although traumatic injury is the leading cause of death in pediatric patients and hemorrhagic shock may be involved in a significant proportion of these deaths, the quality of literature to establish best clinical practices...[and] to develop recommendations... for the care of these patients was lacking.”

National Institute of Child Health & Human Development;R13HDI02128

Hierarchy of Language Utilized in Statements and Recommendations



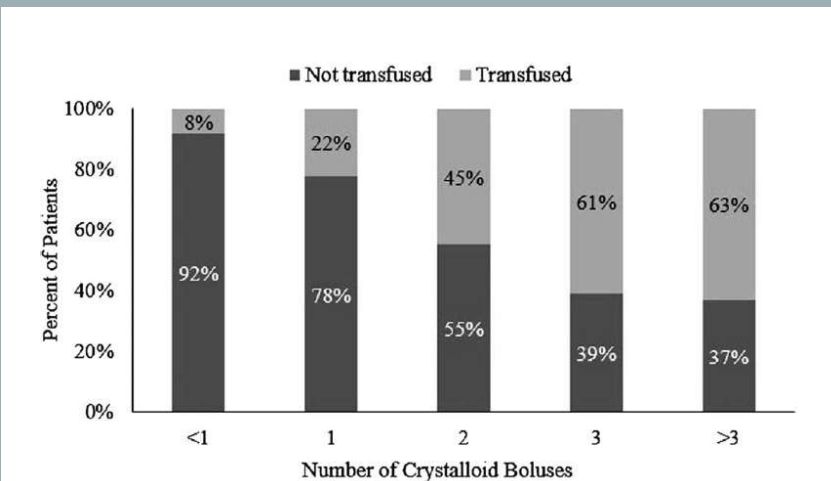
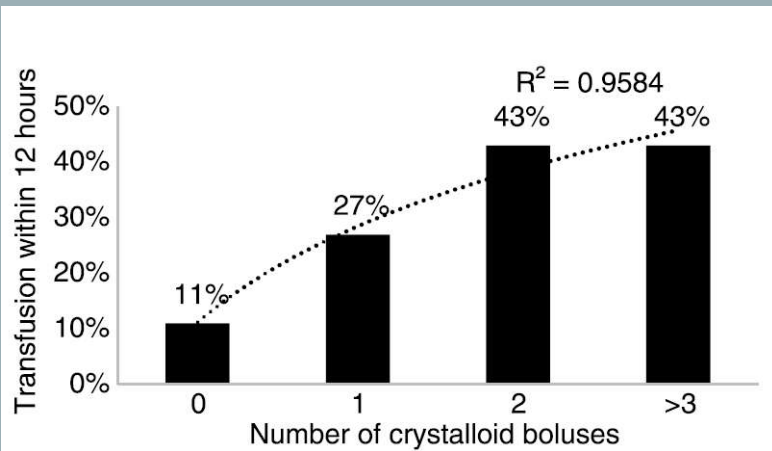


Figure 2. Percentage of patients transfused by number of crystalloid boluses. Patients were significantly more likely to receive blood products with increased number of crystalloid boluses ($p < 0.001$).

TOPIC: USE OF CRYSTALLOID

- We suggest prioritizing the use of blood products over the use of crystalloids for resuscitation

Certainty →	Is recommended
	Should be selected / used
	<u>We suggest</u> is suggested
	Might be considered
	Uncertain whether there is any benefit
	Insufficient evidence

TOPIC: BLOOD PRODUCT RATIOS

- When utilizing blood component resuscitation, we suggest targeting high plasma:RBC ratios (1:1) and high platelet:RBC ratios (1:1) to minimize the plasma and platelet deficits.

24-hour mortality			
	Odds Ratio	95% CI	P value
High plasma:RBC ratio	0.36	0.13-0.99	0.05
Plasma deficit (10mL/kg)	1.2	1.05-1.30	0.01
High platelet:RBC ratio	1.36	0.28-6.66	0.70
Platelet deficit (10mL/kg)	1.1	1.05-1.20	0.04

Spinella et al 2022

FFP:PRBC ratio, continuous	0.42	0.25-0.71
Platelet:PRBC ratio, continuous	0.94	0.51-1.71
FFP:PRBC ratio, categorical		
Low <1:2	1 (Ref)	
Med ≥1:2 & <1:1	0.60	0.39-0.92
High ≥1:1	0.49	0.27-0.87
Platelet:PRBC ratio, categorical		
None 0	1 (Ref)	
Low >0 & <1:2	1.29	0.81-2.05
High ≥1:2	1.04	0.52-2.09

Butler et al 2019

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TOPIC: USE OF LTOWB

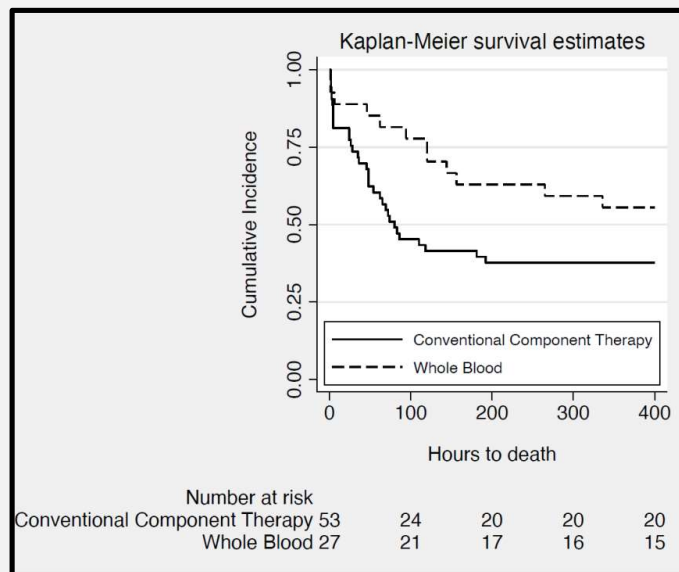
- The use of low titer (≤ 200 Ig G) group O whole blood might be considered if available over individual blood components (RBC, plasma, and platelets) for resuscitation

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.

Anand et al 2020

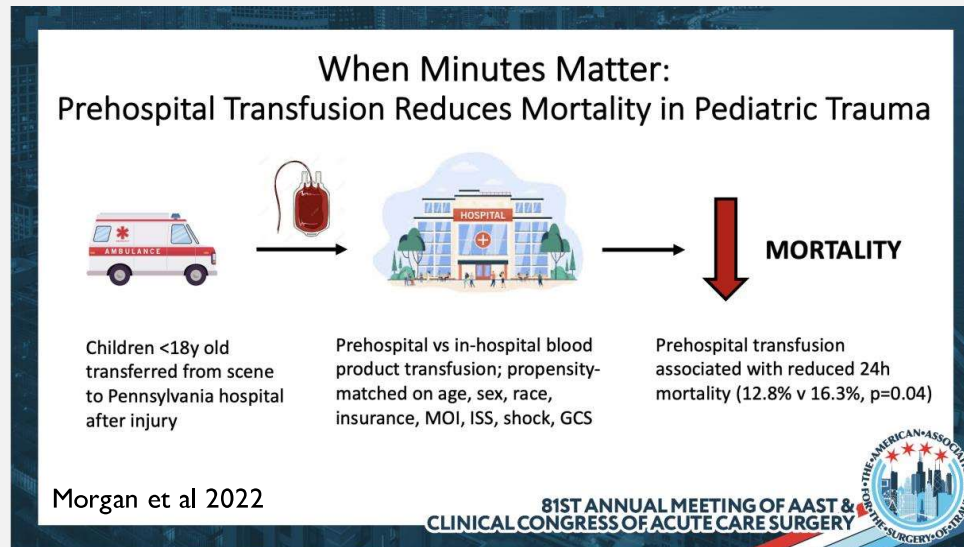


Gaines et al 2020

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Insufficient evidence	

TOPIC: USE OF PRE-HOSPITAL BLOOD PRODUCTS

- There is insufficient evidence to make a recommendation regarding prehospital transfusion. However, it is reasonable to consider prehospital transfusion for injured children based on product availability and clinical judgement.

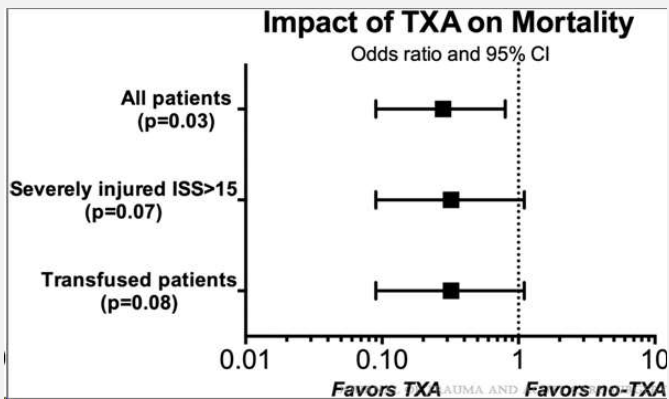


Certainty →	Is recommended
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	We suggest
	Is suggested
	Might be considered
	Uncertain whether there is any benefit
Insufficient evidence	

TOPIC: USE OF TXA AND HEMOSTATIC ADJUNCTS

The empiric use of tranexamic acid within 3 hours of injury might be considered.

n=66



Eckert et al 2014

n=59

Variable	Full Model (n = 400)		Final Model (n = 435)	
	OR	p Value	OR	p Value
AIS (head)	1.47 (1.26–1.71)	<0.0001	1.50 (1.29–1.74)	<0.0001
Age	1.07 (1.00–1.15)	0.34	1.08 (1.01–1.15)	0.032
BD	1.15 (1.09–1.19)	<0.0001	1.15 (1.11–1.19)	<0.0001
Male	0.57 (0.30–1.08)	0.08	1.660 (0.89–3.1)	0.113
TXA+	0.36 (0.12–1.02)	0.055	0.350 (0.12–0.995)	0.0488
Mechanism of injury	0.93 (0.38–2.23)	0.79		
FFP/pRBC ratio	1.26 (0.81–1.96)	0.33		

JOURNAL OF TRAUMA AND ACUTE CARE SURGERY

Hamele et al 2020

Certainty →	Is recommended
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Insufficient evidence	

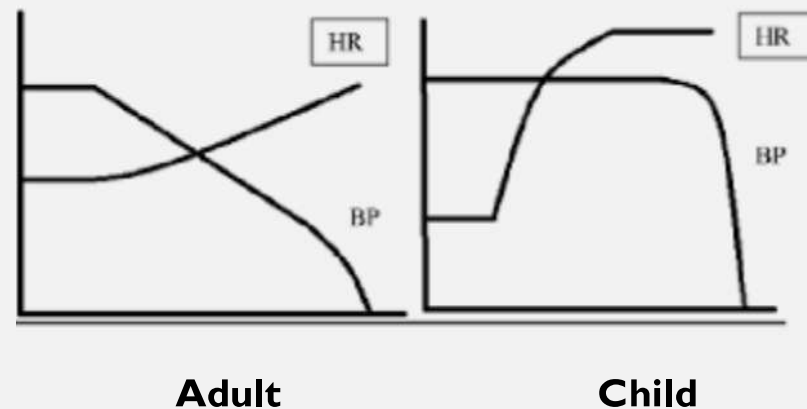
WHY DON'T WE KNOW MORE?

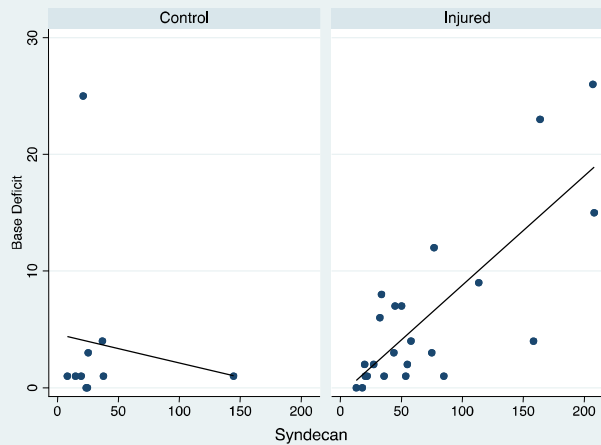
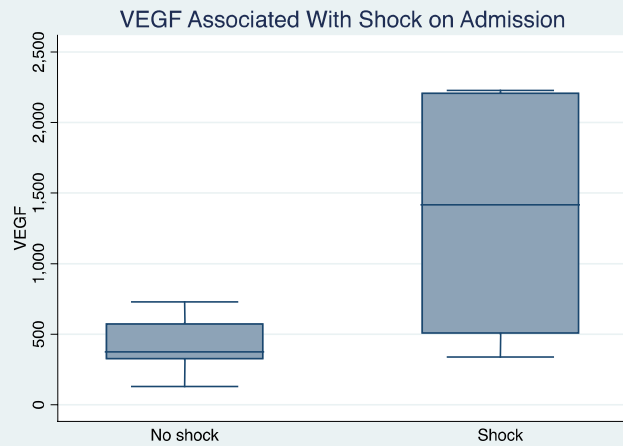
- Emergency research in injured children is challenging & underfunded
- Children are seen as “vulnerable population” → often excluded from research and novel interventions based on the desire to “protect” them
- Very few evidence-based pediatric-specific guidelines to direct hemostatic resuscitation in children
- Pediatric-specific data are desperately needed

RESEARCH PRIORITIES

RESEARCH PRIORITIES: IDENTIFICATION OF HEMORRHAGIC SHOCK

- Improvement in the prompt identification of hemorrhagic shock in pediatric trauma patients
- Scoring systems (ABC, ABCD, SIPA, rSIG) perform poorly in real time
- Which children are bleeding?
- When to activate Massive Transfusion Protocols?





RESEARCH PRIORITIES: MECHANISMS OF COAGULOPATHY

Improved understanding of mechanisms of trauma-induced coagulopathy (TIC)

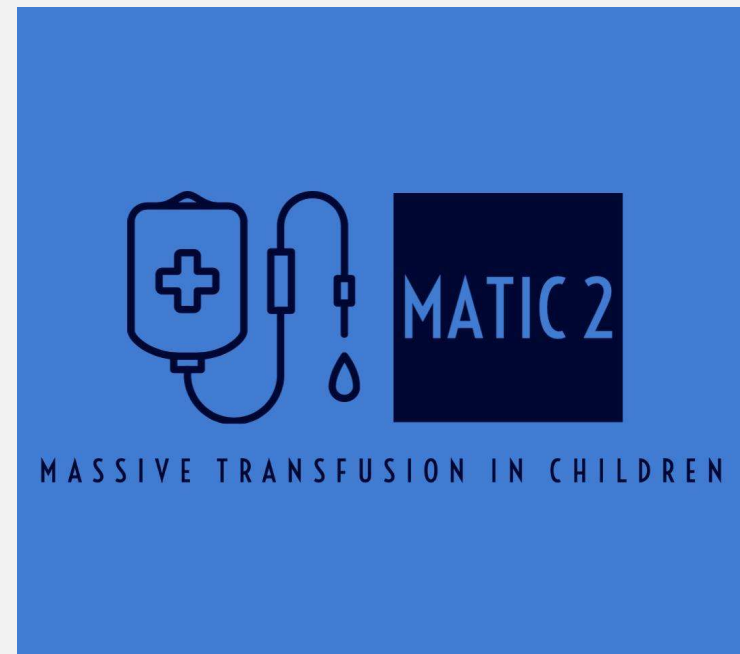
- Maturation of the hemostatic system
- Immunologic response to hemorrhagic shock and transfusion strategies
- Contribution of the endothelium

RESEARCH PRIORITIES: RESUSCITATION STRATEGIES IN HEMORRHAGIC SHOCK

1. To evaluate resuscitation of bleeding pediatric patients with low titer Group O whole blood versus individual blood components
2. To evaluate the safety, efficacy, dosing, and pharmacokinetics of tranexamic acid (TXA) use in pediatric trauma patients.

MASSIVE TRANSFUSION IN CHILDREN - 2 (MATIC-2)

- A pragmatic, randomized, controlled, multicenter (20) trial of 1,000 children with traumatic bleeding
- Aim 1: LTOWB vs component therapy (CT)
- Aim 2: TXA vs placebo
- Aim 3: Multiomics platform



THANK YOU

