Massive Transfusion in Trauma

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Knowledge that will change your world

Disclosures

- None

Objectives

1. What is massive transfusion?

2. Who needs it?

3. Composition of modern massive resuscitation

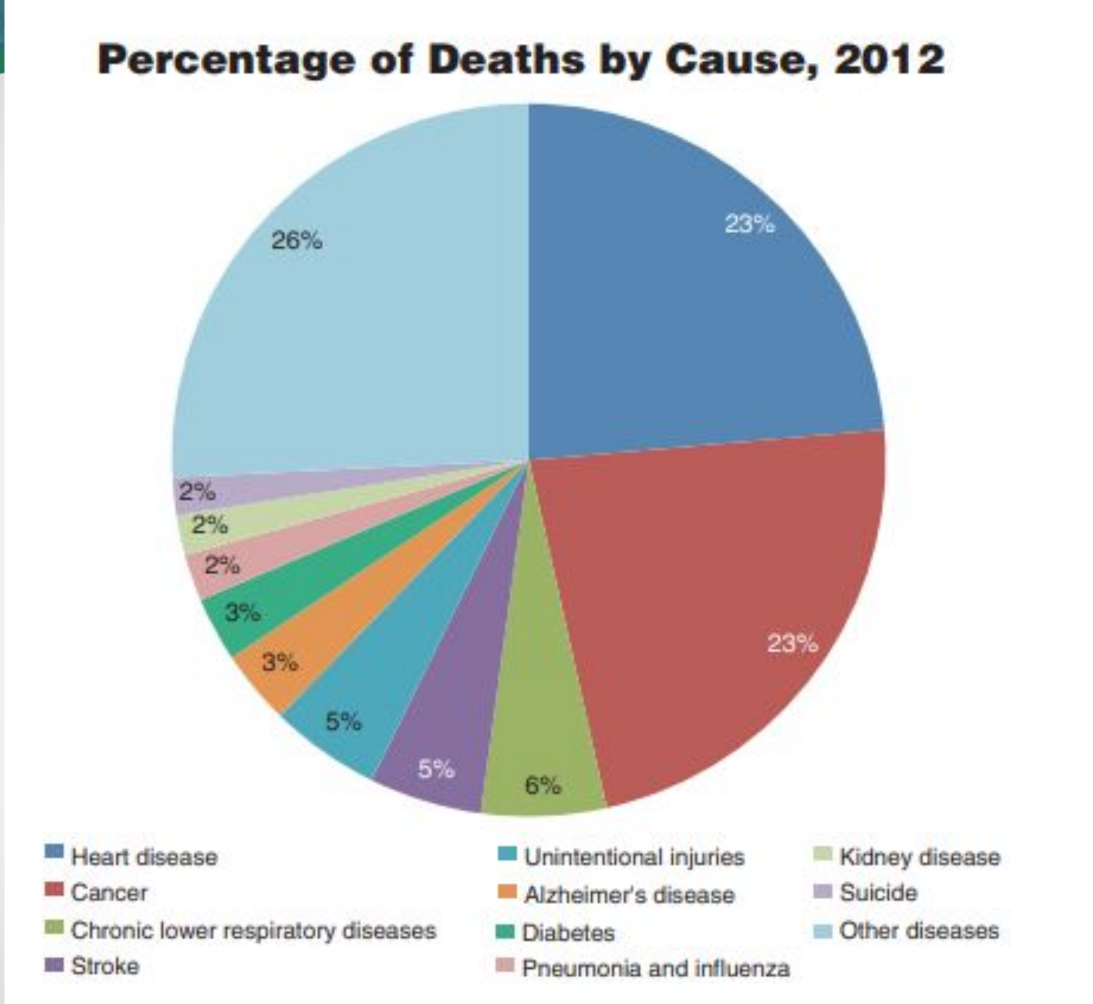
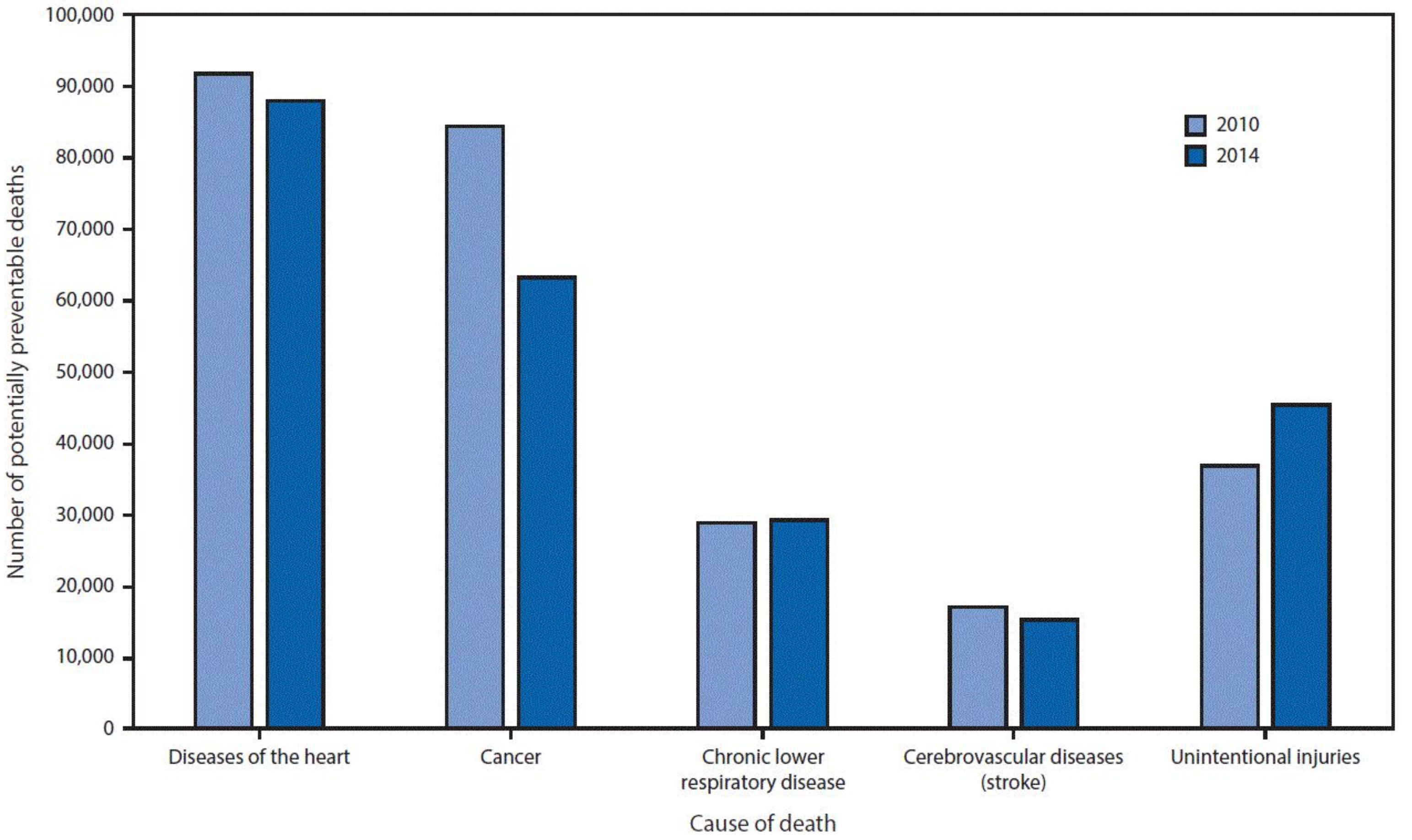
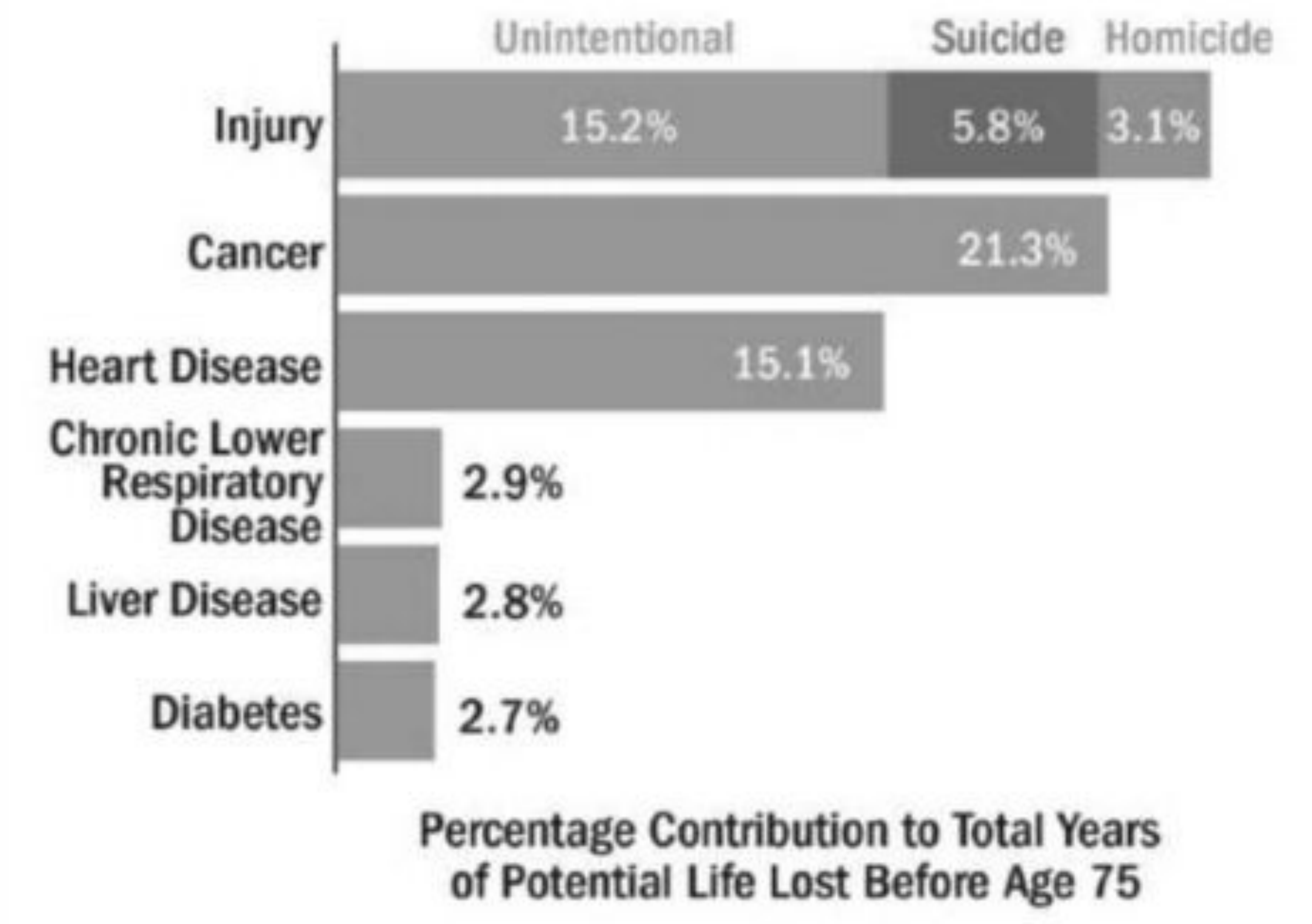

Percentage of Deaths by Cause, 2012
23%
23%
6%
5%
5%
3%
3%
2%
2%
2%
26%
Heart disease
Cancer
Chronic lower respiratory diseases
Stroke
Unintentional injuries
Alzheimer's disease
Diabetes
Pneumonia and influenza
Kidney disease
Suicide
Other diseases

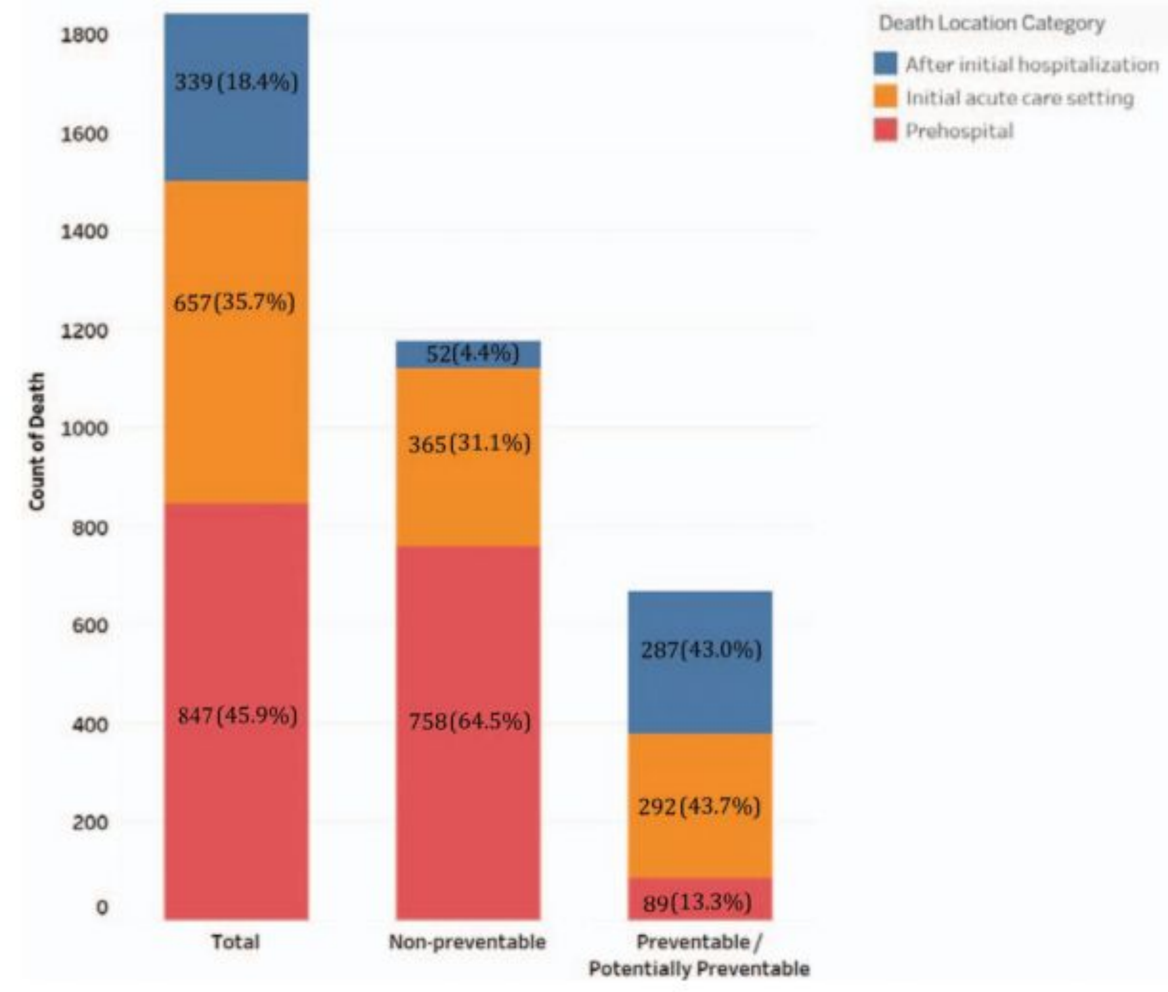
FIGURE. Number of potentially preventable deaths among the five leading causes of death, for persons aged <80 years — United States, 2010 and 2014



García MC, Bastian B, Rossen LM, et al. Potentially Preventable Deaths Among the Five Leading Causes of Death — United States, 2010 and 2014. **MMWR Morb Mortal Wkly Rep** 2016;65:1245–1255. DOI: http://dx.doi.org/10.15585/mmwr.mm6545a1

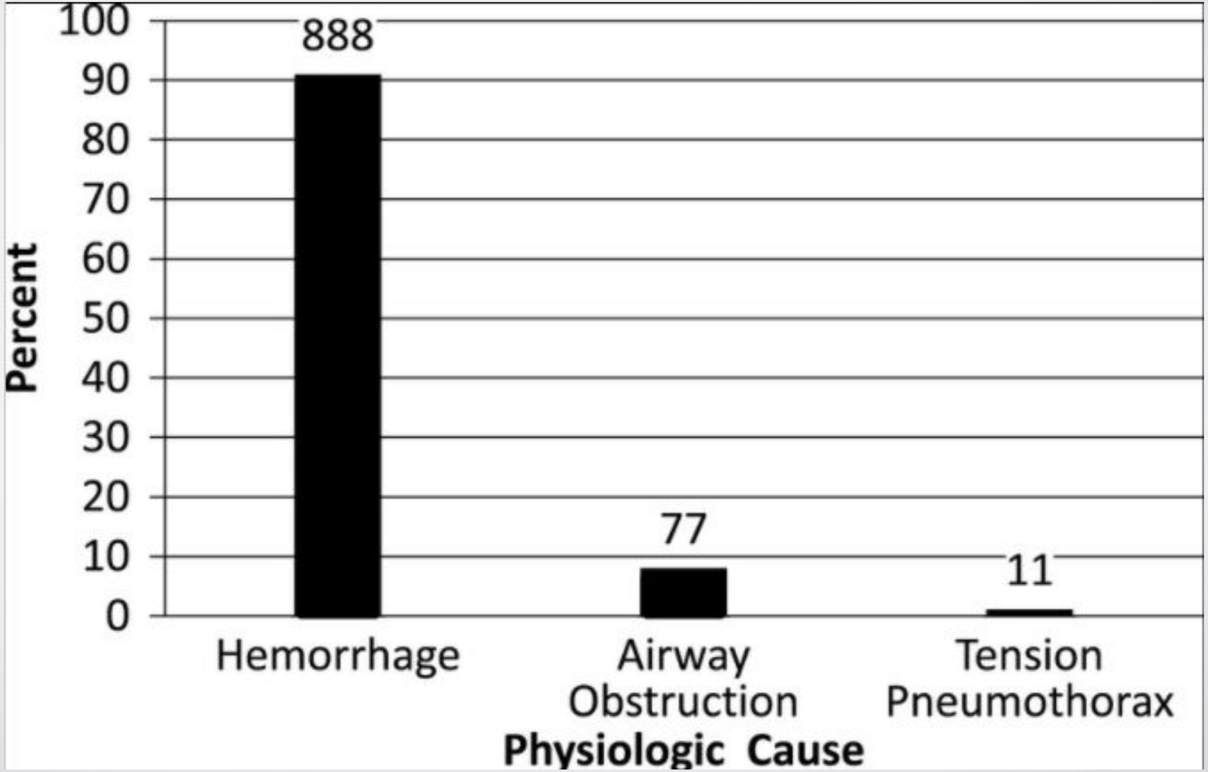


Spinella P and Cap A. Prehospital hemostatic resuscitation to achieve zero preventable deaths after traumatic injury. **Current opinion in hematology**. Nov 2017; 24(6): 529-535.



Drake S, Holcomb J, Yang Y, et al. Establishing a Regional Trauma Preventable/Potentially Preventable Death Rate. **Annals of Surgery**. 2020 Feb; 271(2):375–382

Preventable Death



Eastridge B, Mabry R, Seguin P, et al. Death on the battlefield (2001-2011): Implications for the future of combat casualty care. **J Trauma Acute Care Surg.** 2012 Dec; 73(6): S431-437.

Massive Hemorrhage

General Management

- Rapid control of hemorrhage
- Massive Transfusion
- Limitation of crystalloid

Objectives

1. What is massive transfusion?
2. Who needs it?
3. Composition of modern massive resuscitation

Massive Transfusion

Definition

- Massive transfusion protocol
  - Protocol for deliver of massive transfusion

- Massive transfusion/resuscitation = actual resuscitation

Massive Transfusion

- Rapid, continuous transfusion of blood products
  - Resuscitation
  - Correction of coagulopathy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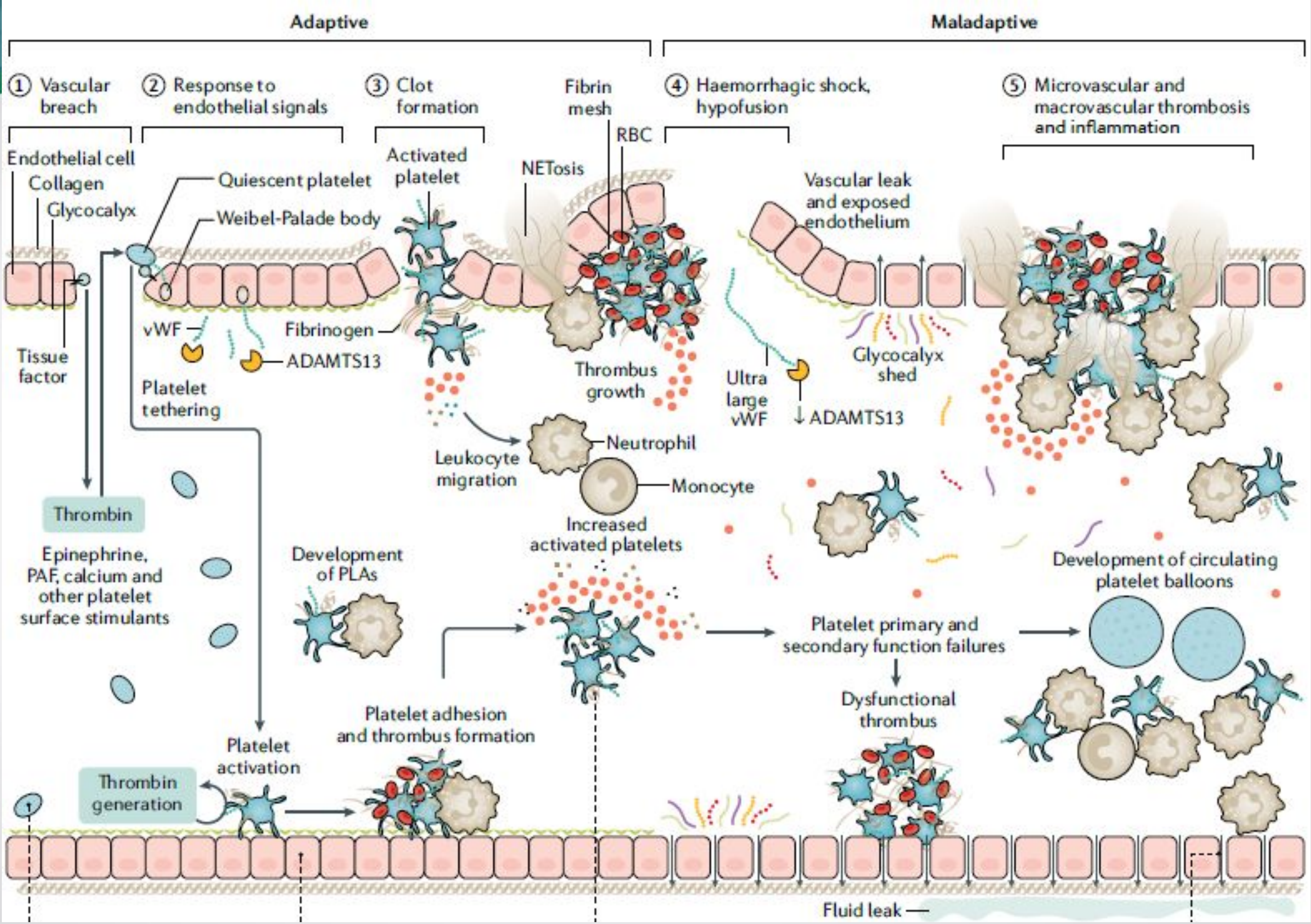
F



Moore EE, Moore HB, Kornblith LZ, et al. Trauma-induced coagulopathy. **Nat Rev Dis Primers.** 2021 Apr; 7(30): 1-23.

Massive Transfusion

- Rapid, continuous transfusion of blood products
- Until control of hemorrhage and correction of coagulopathy
  - Whole blood
  - RBCs
  - FFP
  - Platelets
  - Cryoprecipitate
  - Adjunct agents – TXA, PCC, Ca

Massive Resuscitation

Definition

- Classic definition = ≥ 10 units blood in 24 hours

- Also:
  - ≥ 50 units blood in 48 hours
  - ≥ 20 units blood in 24 hours
  - 50% blood volume within 3 hours
  - ≥ 4 units blood in 4 hours

Massive Resuscitation

Modern definitions

- Critical administration threshold = 3 units RBC per hour
- Resuscitation intensity = 1 point for crystalloid, colloid, any product

Endpoints

- Continue rapid transfusion until bleeding controlled to maintain blood volume
  - Target SBP 100-110 mmHg, avoid <90 mmHg

- May switch to lab based resuscitation with cessation of bleeding and decrease in transfusion requirement
  - Visicoelastic testing preferable to standard coagulation assays
  - Trend labs (lactate, base excess, etc), clinical parameters

Wolley T, Thompson P, Kirkman E, et al. Trauma hemostasis and oxygenation research network position paper on the role of hypotensive resuscitation as part of remote damage control resuscitation. **J Trauma Acute Care Surg.** 2018 Feb; 84(6): S3-S13.
ACS TQIP Massive Transfusion in Trauma Guidelines. 2014 Oct. https://www.facs.org/-/media/files/quality-programs/trauma/tqip/transfusion_guildelines.ashx

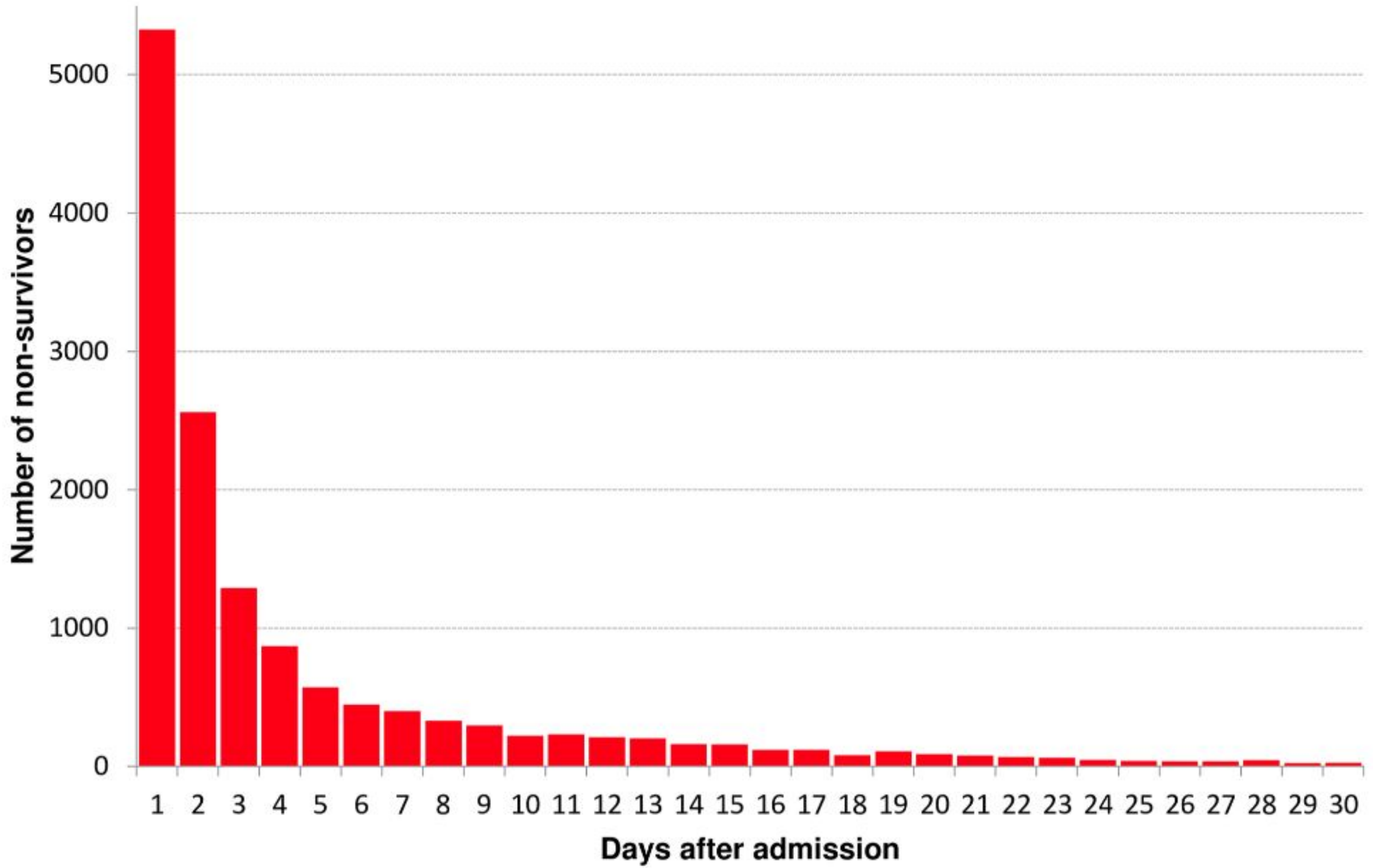
Time to Death with Hemorrhage

TABLE 2. Outcomes of Patients Requiring Emergent OR/IR (N = 468)

Variables	Group 1 (n = 102)	Group 2 (n = 102)	Group 3 (n = 104)	Group 4 (n = 100)	Group 5 (n = 60)	p*
Transfusions during active resuscitation						<0.01
RBC (units)	5 (4, 8)	7 (4, 11)	8 (5, 14)	13 (8, 24)	20 (11, 37)	
Plasma (units)	2 (1, 3)	3 (2, 6)	5 (2, 10)	8 (4, 15)	14 (6, 20)	
Platelets (units)	1 (0, 1)	1 (0, 2)	1 (1, 2)	2 (1, 3)	3 (1, 4)	
Mortality at 6 h (n, %)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	55 (92%)	1.00
Mortality at 24 h (n, %)	1 (1%)	2 (2%)	2 (2%)	1 (%)	59 (98%)	1.00
Mortality at 30 d (n, %)	8 (8%)	8 (8%)	8 (8%)	15 (15%)	60 (100%)	0.25
Time to death (d)	3.6 (1.3, 6.3)	2.8 (0.8, 11.9)	7.1 (1.5, 18.5)	8.8 (2.5, 11.2)	0.09 (0.05, 0.15)	0.74

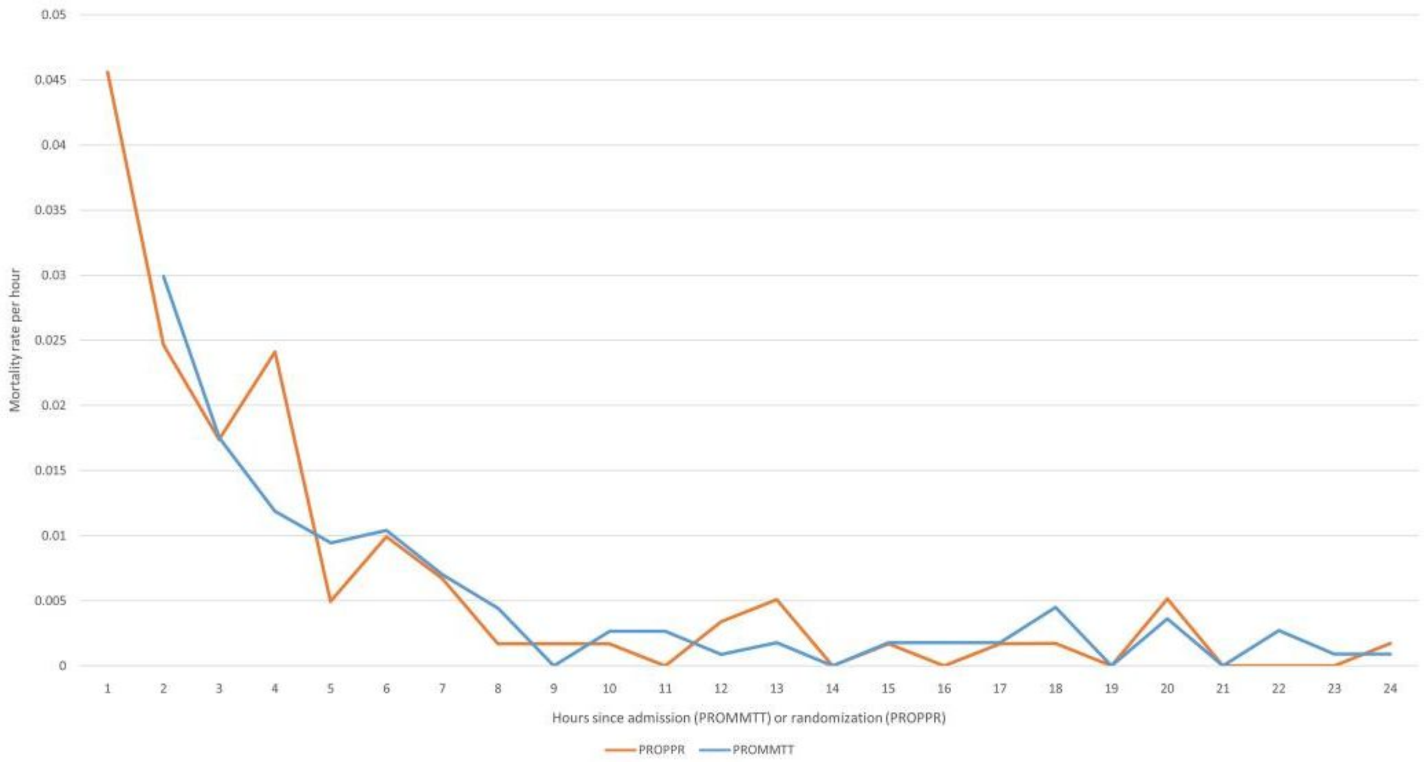
- Median time of death = 2.2 hours

Chang R, Kerby J, Kalkwarf K et al. Earlier time to hemostasis is associated with decreased mortality and rate of complications: Results from the Pragmatic Randomized Optimal Platelet and Plasma Ratio trial. **J Trauma Acute Care Surg**. 2019 Aug; 87(2): 342-349.



Rauf R, von Matthey F, Croenlein, et al. Changes in the temporal distribution of in-hospital mortality in severely injury patients-An analysis of the TraumaRegister DGU. **PLoS One.** 2019 Feb; 14(2): e0212095.

Time to Death with Hemorrhage



Fox E, Holcomb J, Wade C, et al. Earlier endpoints are required for hemorrhagic shock trials among severely injured patients. **Shock.** 2018 May; 47(5): 567-573.
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Objectives

1. What is massive transfusion?

2. Who needs it?

3. Composition of modern massive resuscitation

Population

Always assume hemorrhage until proven otherwise

- Start massive transfusion protocol empirically
- Don’t delay activation in unstable patient while awaiting confirmation of hemorrhage

Population

Who requires massive transfusion?

- 3-5% of all trauma patients require massive transfusion

Predictors

- ABC score
- Shock index
- Penetrating injury
- HR ≥ 120 bpm
- SBP < 90 mmHg
- GCS < 9

Nunez TC, Voskresensky IV, Dossett LA, et al. Early prediction of massive transfusion in trauma: simple as ABC (Assessment of Blood Consumption)? **J Trauma Acute Care Surg.** 2009 Feb; 66(2): 346-352.
Rainer TH, Ho AM, Yeung JH, et al. Early risk stratification of patients with major trauma requiring massive blood transfusion. **Resuscitation.** 2011 June; 82(6): 724-729.

Objectives

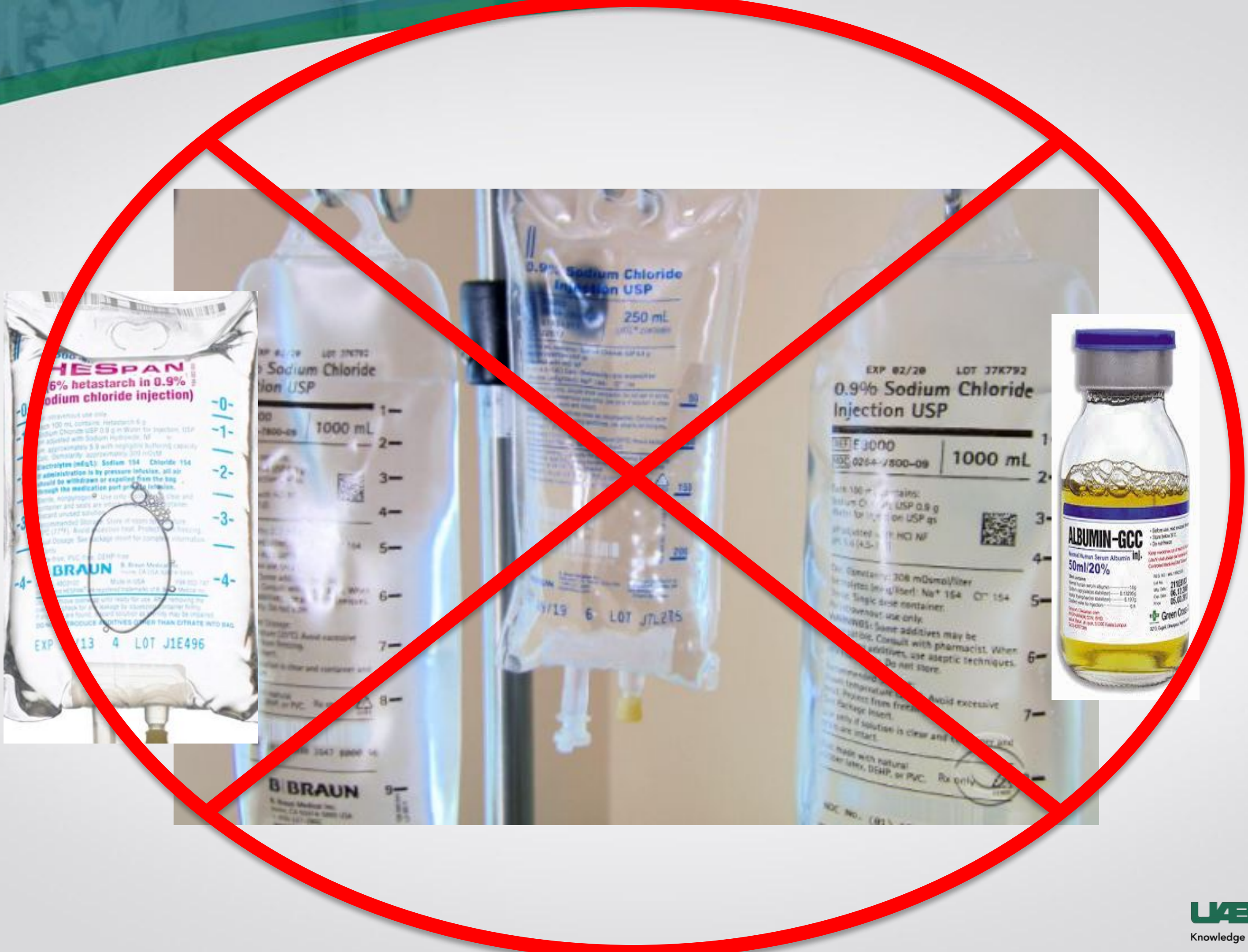
1. What is massive transfusion?

2. Who needs it?

3. Composition of modern massive resuscitation

Massive Transfusion

- Blood product resuscitation
  - Whole blood
  - RBCs
  - FFP
  - Platelets
  - Cryoprecipitate
  - Adjunct agents – TXA, PCC, Ca
- Limitation of crystalloid/colloid products


HESPAN
(6% hetastarch in 0.9% Sodium chloride injection)
B BRAUN
EXP 02/20 LOT 37K792
0.9% Sodium Chloride Injection USP
1000 mL
0.9% Sodium Chloride Injection USP
250 mL
B BRAUN
ALBUMIN-GCC
50ml/20%

1970s-2000s

Classification of Hemorrhagic Shock				
	Class I	Class II	Class III	Class IV
Blood Loss (%)	<15%	15-30%	31-40%	>40%
Heart rate	60-100	101-120	121-140	>140
Blood Pressure	Normal	Normal	Decreased	Decreased
Mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic
Fluid requirements	Crystalloid	Crystalloid	Crystalloid, blood products	Crystalloid, blood products

World War II	Korean War	Vietnam
0.9 to 1.1	1.9 to 5.5	4.0 to 5.0
avg 1 unit/ casualty	avg 2 units/ casualty	avg 4.4 units/ casualty

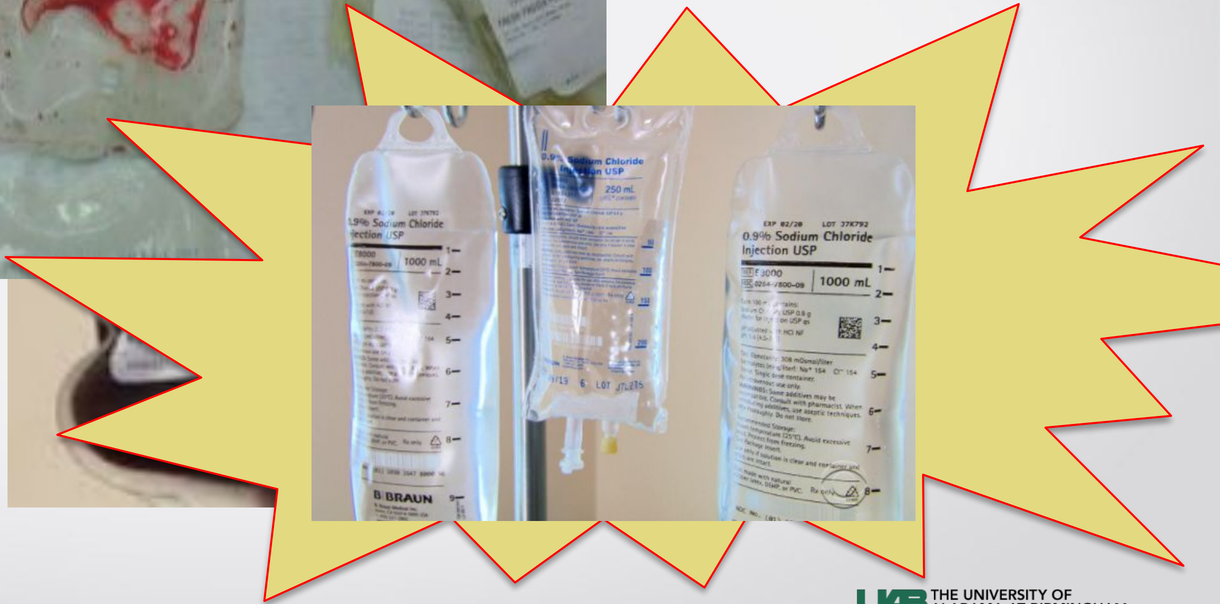
Outcomes

Hospital mortality rate:

- World War 2 = 4.5%
- Korea = 2.5%
- Vietnam = 2.6%

Neel S. Medical support of the US Army in Vietnam 1965-1970. Department of the Army. 1991.

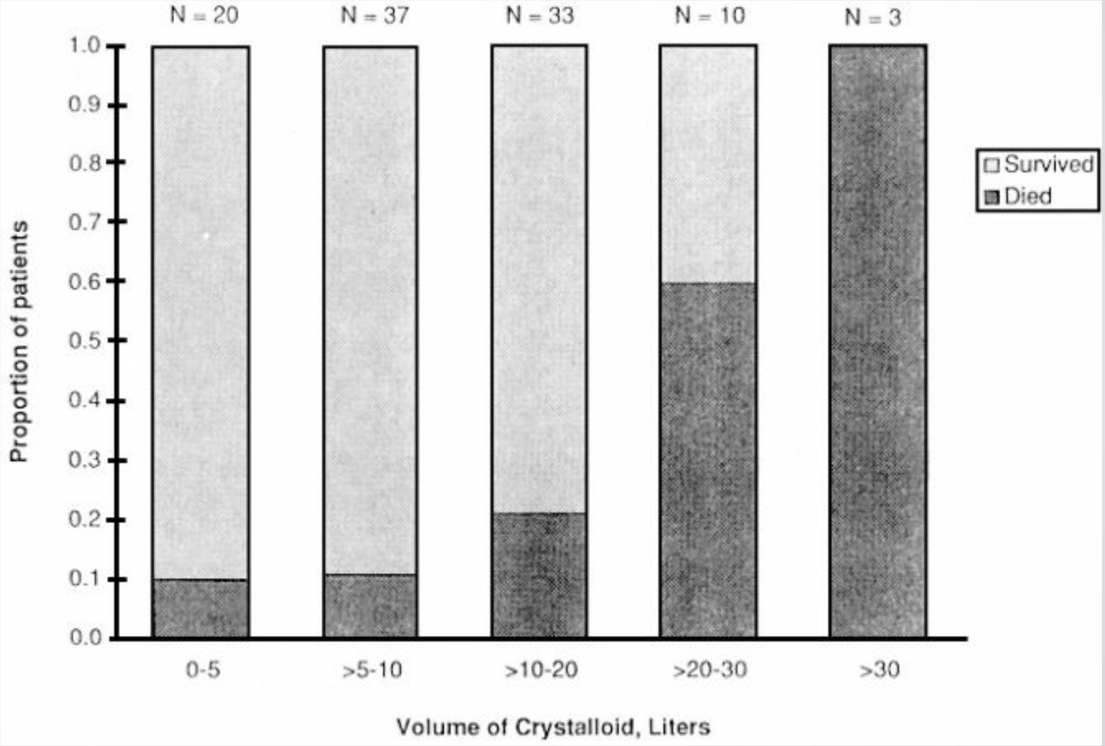
0.9% Sodium Chloride Injection USP
B



0.9% Sodium Chloride Injection USP
1000 mL
0.9% Sodium Chloride Injection USP
250 mL
0.9% Sodium Chloride Injection USP
1000 mL
B BRAUN

Mortality rates

- 1970s: 90%
- 1980s: 80%
- 1990s: 50%



Cinat M, Wallace W, Nastanski F, et al. Improved survival following massive transfusion in patients who have undergone trauma. **Arch Surg.** 1999; 134(9): 964-968.
Heckbert S, Vedder N, Hoffman W, et al. Outcome after hemorrhagic shock in trauma patients. **J Trauma.** 1998 Sept; 45(3): 545-549.

Reasons for Change

- Infectious complications
- Concern over blood utilization and waste
- Technological advances
- Limited evidence supporting crystalloid use

Transfusion concerns

- Hepatitis with plasma transfusion
  - World War 2: 7.5%
  - Korean War: 21%
  - Vietnam: 3.6-8%
- HIV/AIDS
- HTLV-1

Neel S. Medical support of the US Army in Vietnam 1965-1970. Department of the Army. 1991..

Blood Utilization

- 20% of patients crossmatched actually transfused
- Nearly 50% product waste rate

Neel S. Medical support of the US Army in Vietnam 1965-1970. Department of the Army. 1991..

Technological Advances

- 1964: Plasmapheresis allowing fractionation
- 1965: cryoprecipitate production
- 1969: platelet storage at room temperature
- 1972: Apheresis used to extract one cellular component and return rest
- 1983: Shelf life of red blood cells increased to 42 days.

Blood Storage

- Whole blood = 21 days
- RBCs = 42 days
- FFP = 1-7 years
- Platelets = 5 days

Progressive Hypovolemia Leading to Shock after Continuous Hemorrhage and 3:1 Crystalloid Replacement

April 1964

Fluid Therapy in Hemorrhagic Shock

TOM SHIRES, MD; DALE COLN, MD; JAMES CARRICO, MD; et al

» Author Affiliations

Arch Surg. 1964;88(4):688-693. doi:10.1001/archsurg.1964.01310220178027

Hemostasis in Massively Transfused Trauma Patients

R. B. COUNTS, C. HAISCH, T. L. SIMON, N. G. MAXWELL, D. M. HEIMBACH, C. J. CARRICO

Benefits of Crystalloid

- Easy to store
- Cheap and available
- Familiar and presumed safe

Results

- Availability of invasive monitoring and new endpoints

- Crystalloid can be used to expand extracellular volume with later contraction

- Fluid shift into interstitium regardless of blood loss

- Less emphasis on FFP, platelets in blood resuscitation

Cantle P and Cotton B. Balanced resuscitation in trauma management. **Surg Clin N Am 97.** 2017; 2017: 964-968.

Complications of Crystalloid

- Acidotic
- Coagulopathic
- Volume overload and edema
  - ARDS
  - Abdominal compartment syndrome
  - Decreased renal perfusion
  - Decreased cardiac contractility
  - Instestinal dysmotility

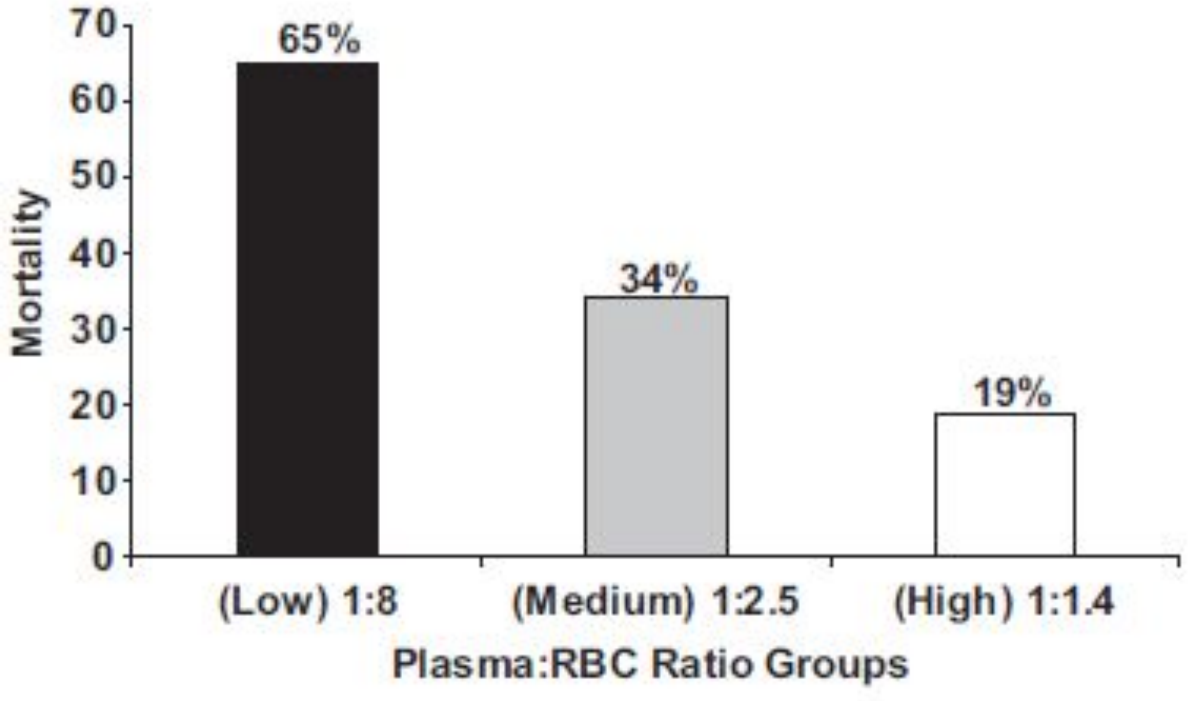
Cantle P and Cotton B. Balanced resuscitation in trauma management. **Surg Clin N Am 97.** 2017; 2017: 964-968.

f Crystalloid

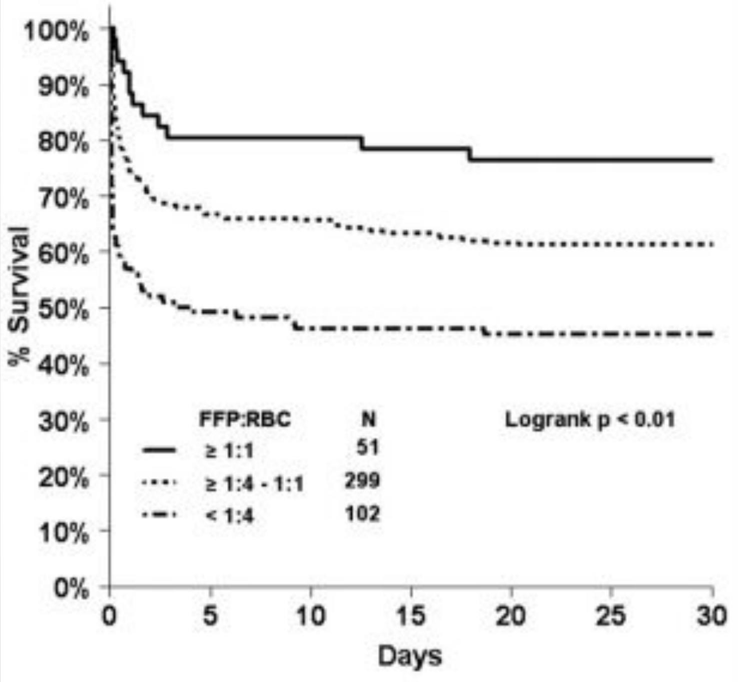
Burlew CC. The open abdomen: practical implications for the practicing surgeon. **Am J Surg.** 2012; 204: 826-835.

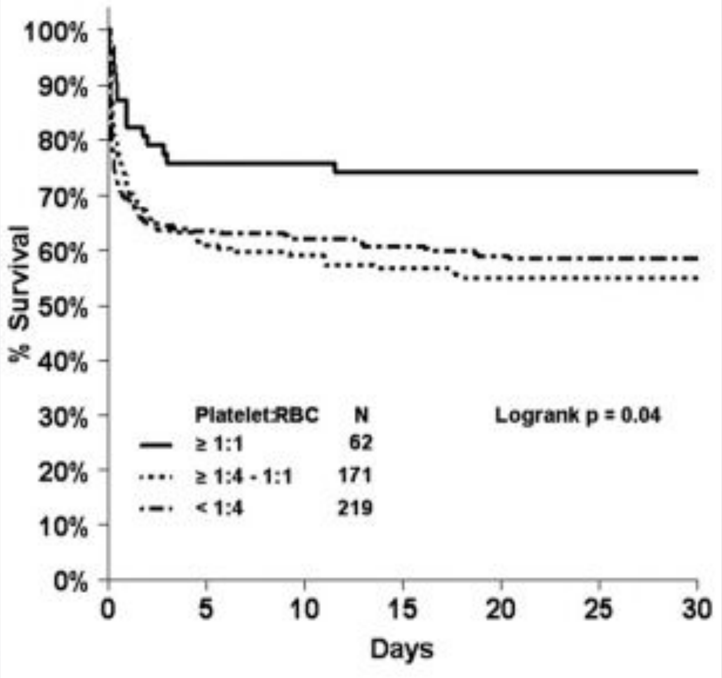
The Ratio of Blood Products Transfused Affects Mortality in Patients Receiving Massive Transfusions at a Combat Support Hospital

Matthew A. Borgman, MD, Philip C. Spinella, MD, Jeremy G. Perkins, MD, Kurt W. Grathwohl, MD, Thomas Repine, MD, Alec C. Beekley, MD, James Sebesta, MD, Donald Jenkins, MD, Charles E. Wade, PhD, and John B. Holcomb, MD



Borgman M, Spinella P, Perkins J, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma Acute Care Surg. 2007;63: 805-813.





Zink K, Sambasivan C, Holcomb J, Chisholm, Schreiber M. A high ratio of plasma and platelets to packed red blood cells in the first 6 hours of massive transfusion improves outcomes in a large multicenter study. **Am J Surg**. 2009; 197: 565-570.

Damage Control Hematology: The Impact of a Trauma Exsanguination Protocol on Survival and Blood Product Utilization

Bryan A. Cotton, MD, Oliver L. Gunter, MD, James Isbell, MD, Brigham K. Au, BS, Amy M. Robertson, MD, John A. Morris, Jr., MD, Paul St. Jacques, MD, and Pampee P. Young, MD, PhD

Optimizing Outcomes in Damage Control Resuscitation: Identifying Blood Product Ratios Associated With Improved Survival

Oliver L. Gunter, Jr., MD, Brigham K. Au, BS, James M. Isbell, MD, Nathan T. Mowery, MD, Pampee P. Young, MD, PhD, and Bryan A. Cotton, MD

Postinjury Life Threatening Coagulopathy: Is 1:1 Fresh Frozen Plasma: Packed Red Blood Cells the Answer?

Jeffry L. Kashuk, MD, Ernest E. Moore, MD, Jeffrey L. Johnson, MD, James Haenel, RRT, Michael Wilson, MD, John B. Moore, MD, C. Clay Cothren, MD, Walter L. Biffl, MD, Anirban Banerjee, PhD, and Angela Sauaia, MD, PhD

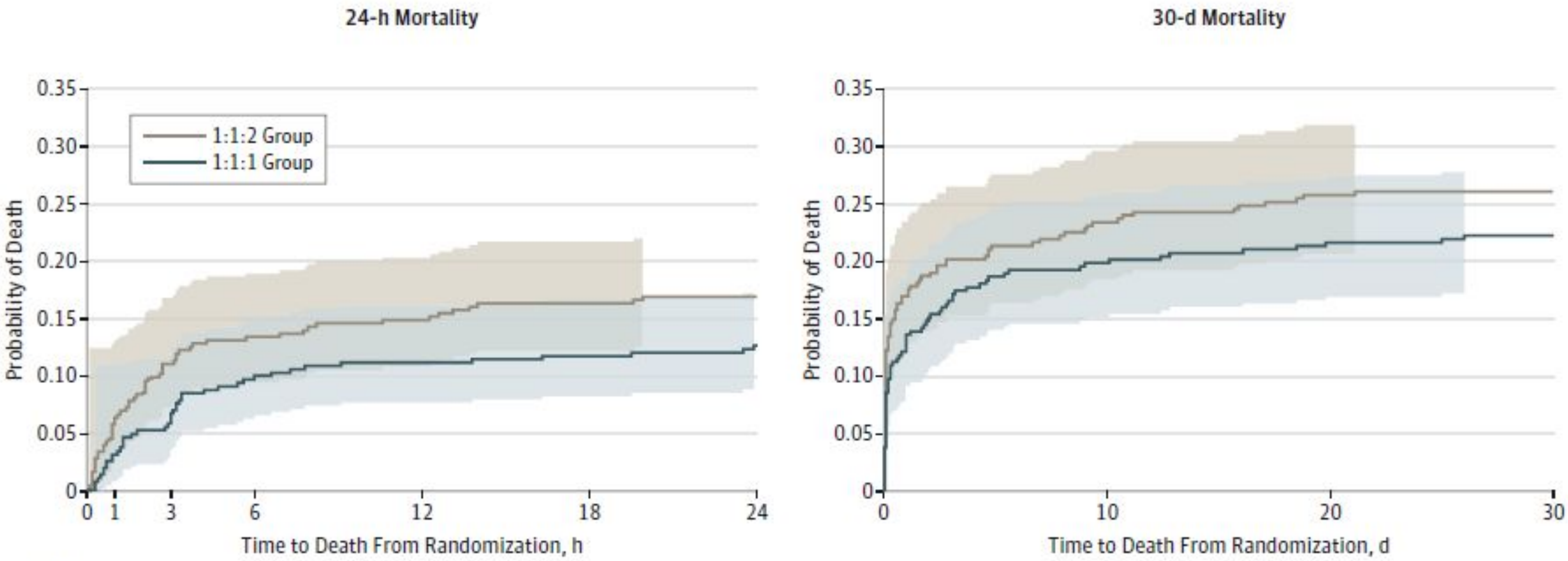
Review of Current Blood Transfusions Strategies in a Mature Level I Trauma Center: Were We Wrong for the Last 60 Years?

Juan C. Duchesne, MD, John P. Hunt, MD, MPH, Georgia Wahl, MD, NREMT-P, Alan B. Marr, MD, Yi-Zarn Wang, DDS, MD, Sharon E. Weintraub, MD, MPH, Mary J. O. Wright, MD, and Norman E. McSwain, Jr., MD

Fresh Frozen Plasma Should be Given Earlier to Patients Requiring Massive Transfusion

Ernest A. Gonzalez, MD, Frederick A. Moore, MD, John B. Holcomb, MD, Charles C. Miller, PhD, Rosemary A. Kozar, MD, PhD, S. Rob Todd, MD, Christine S. Cocanour, MD, Bjorn C. Balldin, MD, and Bruce A. McKinley, PhD

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma
The PROPPR Randomized Clinical Trial

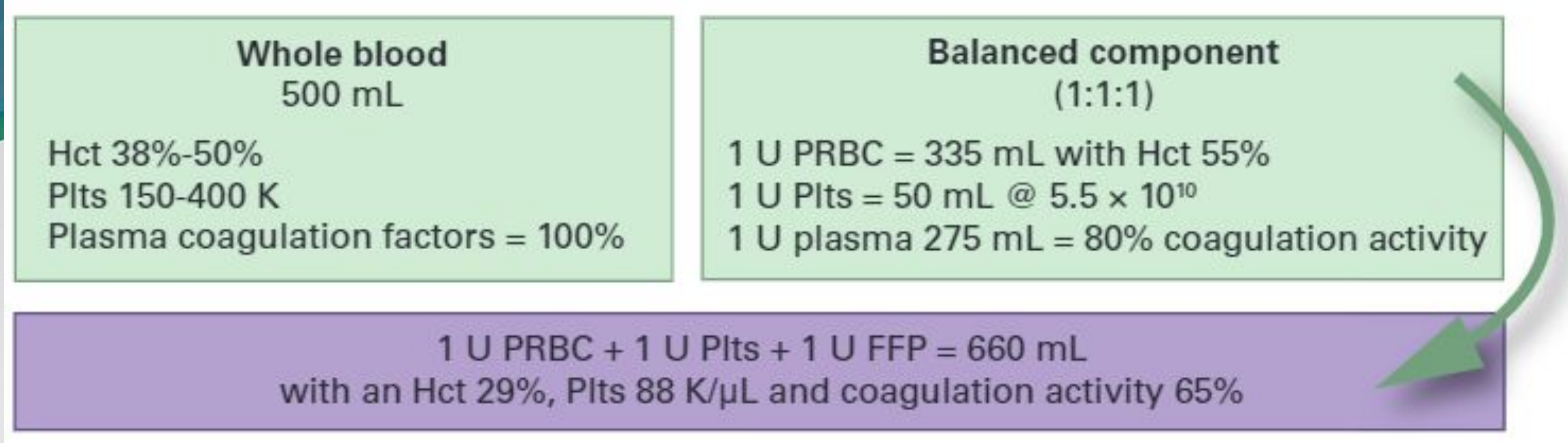


No. at risk

1:1:2	342	322	304	296	291	286	284	342	261	253	252
1:1:1	338	327	318	305	300	297	295	338	269	263	260

Advances and adjunctive agents

- Whole blood
- TXA
- Ca
- PCC



- Multiple preservatives
  - Dextrose Mannitol Sodium phosphate
  - Adenine Sodium citrate

- Possible improvement in outcomes

D'Angelo M and Dutton RP. Management of trauma-induced coagulopathy: Trends and practices. AANA journal; Jan 2010. 78(1):35-40

Types of Whole Blood

Fresh Whole Blood vs Component Therapy

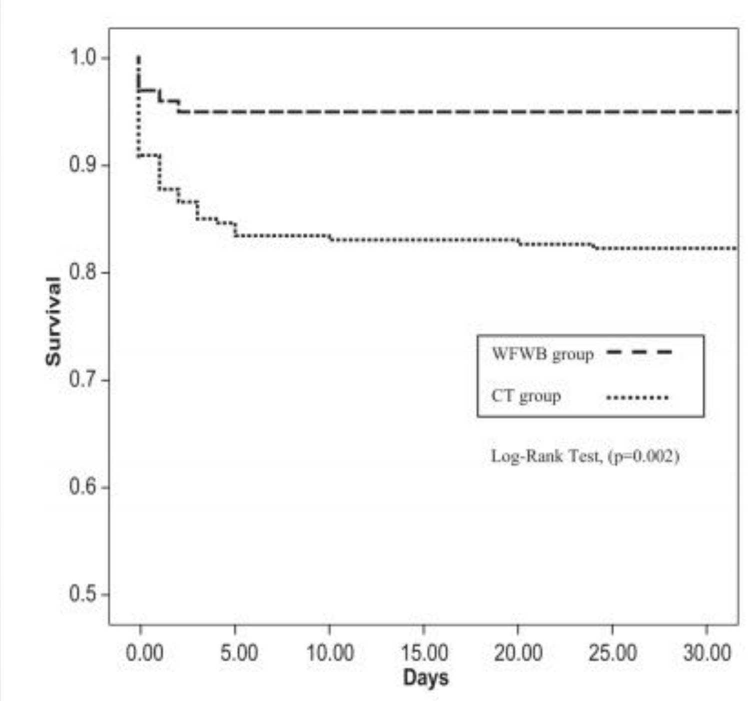


TABLE 6. Propensity score used as continuous variable in logistic regression predicting effect of FWB on death

	Odds ratio	95% CI	p Value
FWB use	0.096	0.02,0.53	0.008
Injury Severity Score	1.07	1.03,1.11	<0.001
Glasgow Coma Score	0.72	0.65,0.79	<0.001
Propensity score	9.72	1.45,64.97	0.019

Arrival systolic blood pressure, arrival temperature, use of factor VIIa, total red blood cells, and total plasma administered were used to calculate propensity score.

CI = confidence interval; FWB = fresh whole blood.

Spinella P, Perkins J, Grathwohl, Beekley A, Holcomb J. Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries. **J Trauma.** 2009**;** 66(4 Suppl): S69-S76.

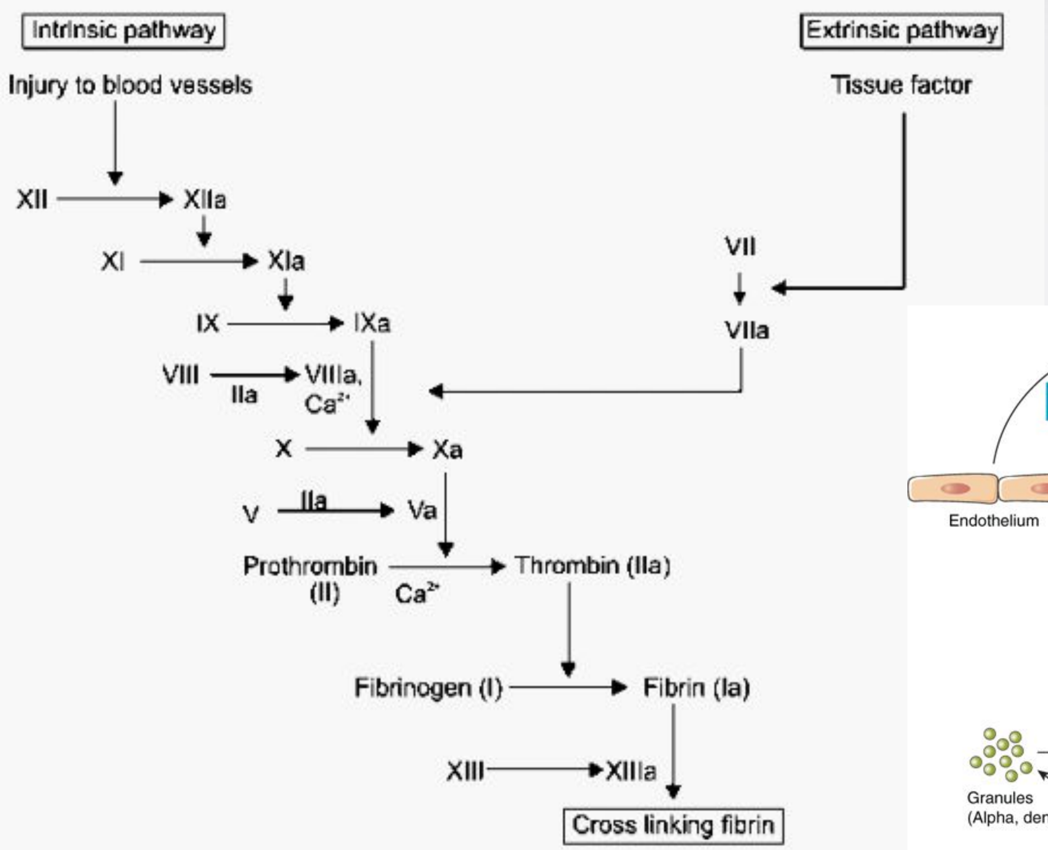
Nessen S, Eastridge B, Cronk D, et al. Fresh whole blood use by forward surgical teams in Afghanistan is associated with improved survival compared to component therapy without platelets. **Transfusion.** 2013 Jan; 53: 107S-113S.

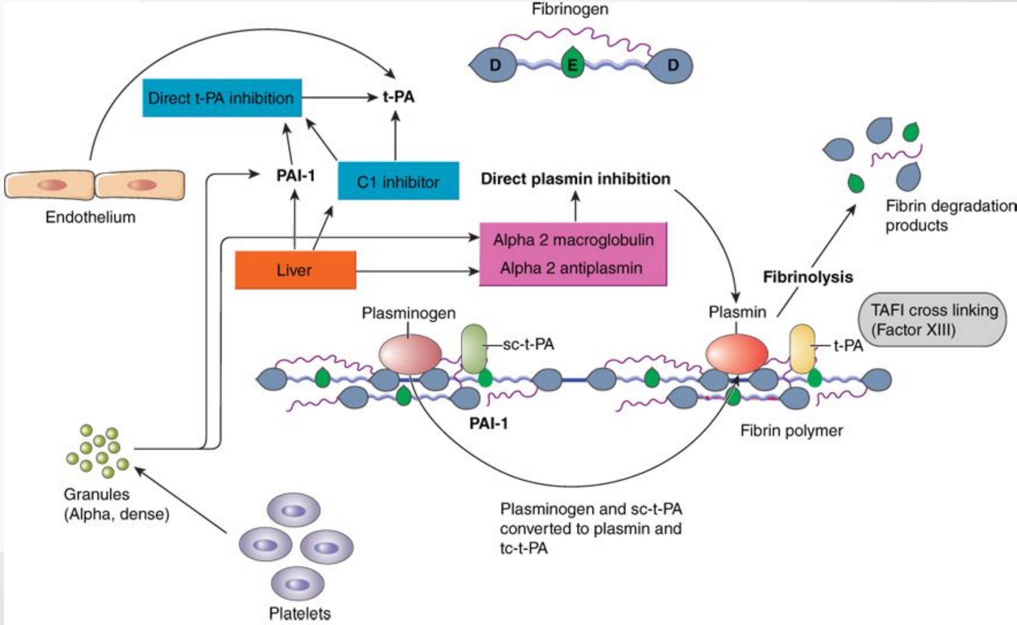
Warm Fresh Whole Blood

- Likely an unattainable ideal for civilian trauma
  - Requires large enough available walking blood bank
  - Prescreened and immunized to hepatitis B
  - Increased risk of hepatitis C transmission (1:96,000 vs 1:1,000,000)
  - Increased risk of HIV transmission

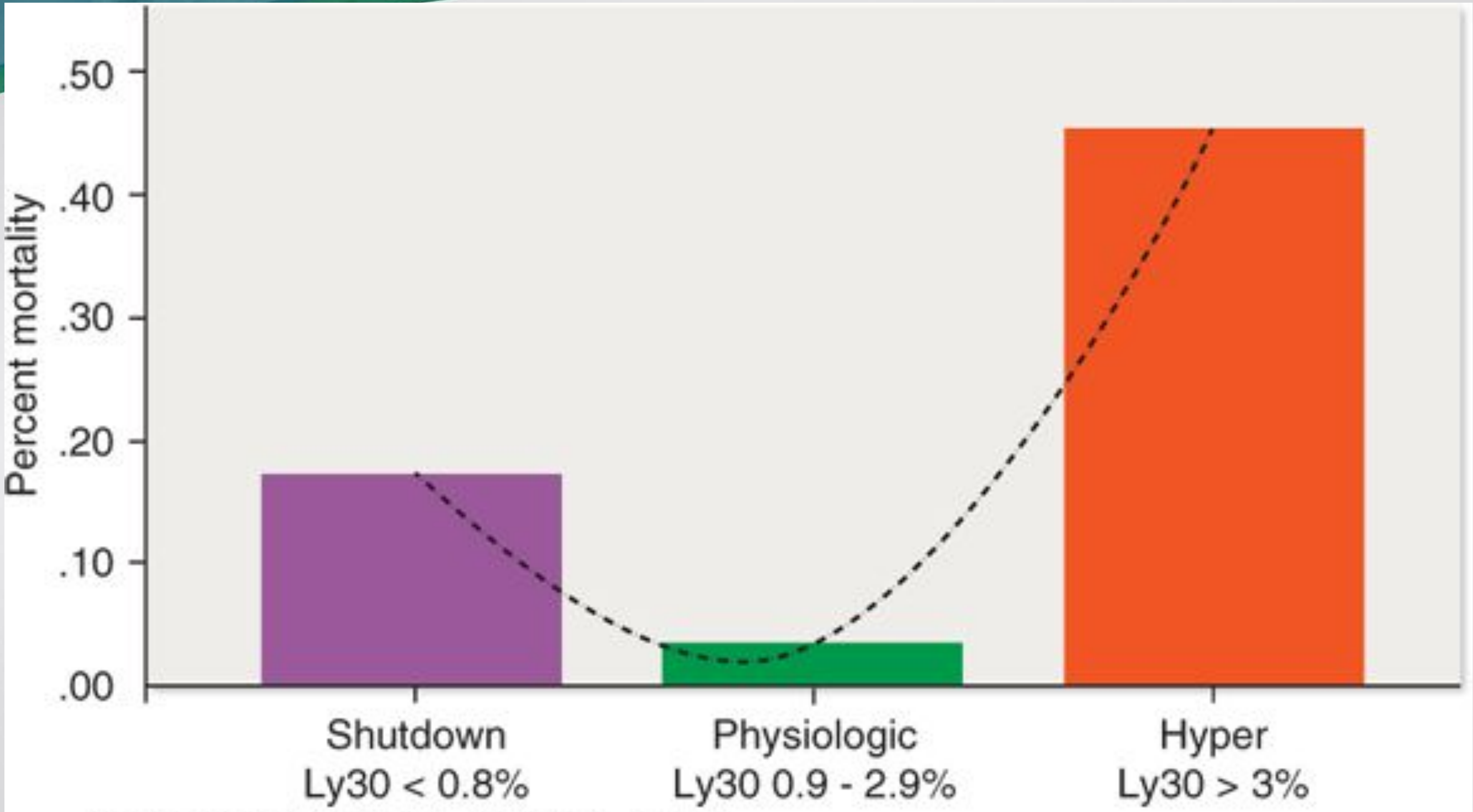
Stored Whole Blood

- Increasing popularity in civilian trauma
- No definitive evidence
    - Small, retrospective studies suggesting improvement in mortality
- Planned prospective, RCT comparing cold, stored whole blood and component therapy





Source: David V. Feliciano, Kenneth L. Mattox, Ernest E. Moore: Trauma, Ninth Edition



Moore H, Moore E, Gonzalez E, et al. Hyperfibrinolysis, physiologic fibrinolysis, and fibrinolysis shutdown: the spectrum of postinjury fibrinolysis and relevance to antifibrinolytic therapy. **J Trauma Acute Care Surg.** 2014; 77: 811-817.

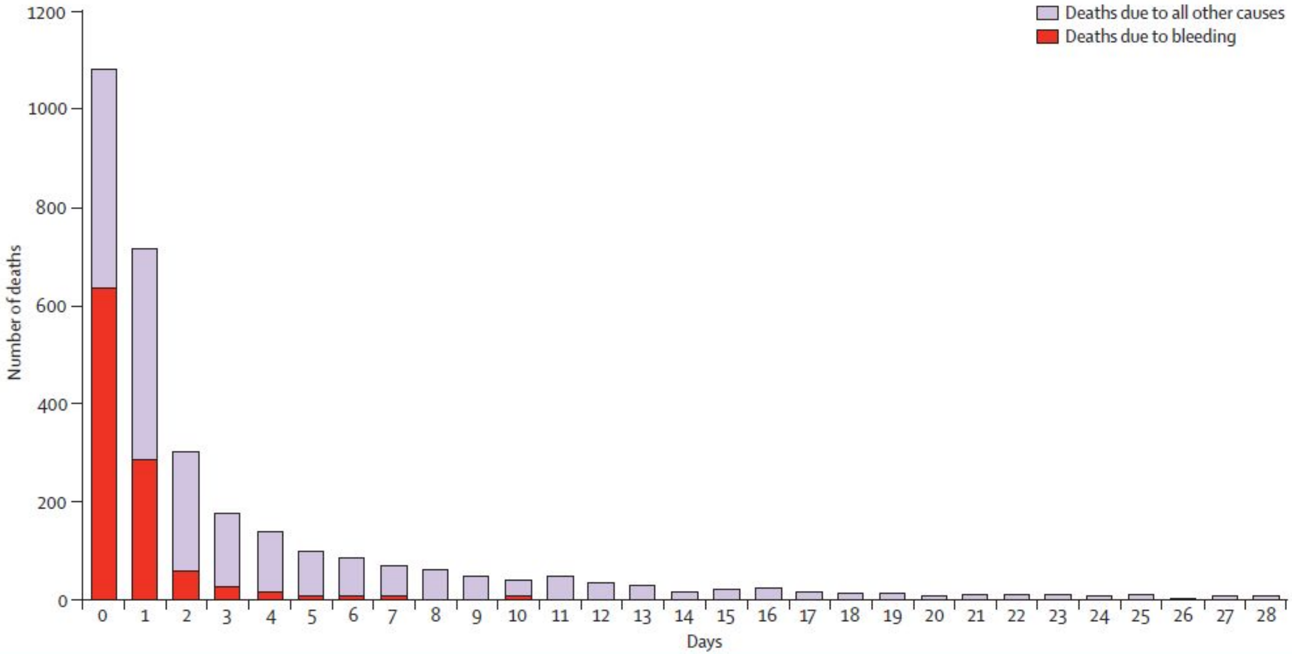


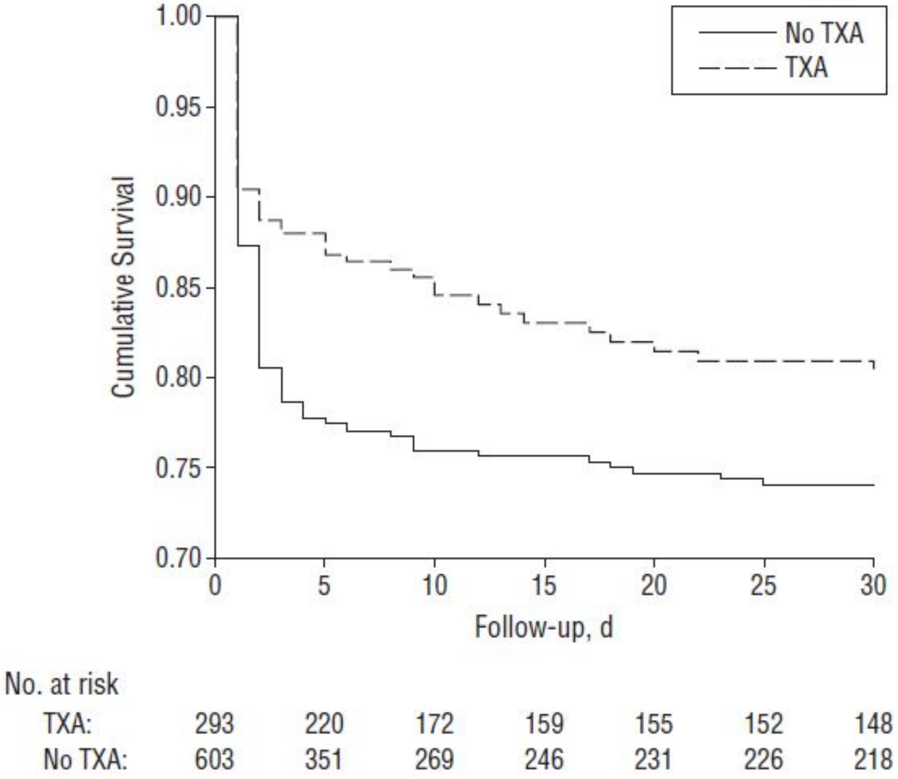
Figure 2: Mortality by days from randomisation

	Tranexamic acid (n=10 060)	Placebo (n=10 067)	RR (95% CI)	p value (two-sided)
Any cause of death	1463 (14·5%)	1613 (16·0%)	0·91 (0·85–0·97)	0·0035
Bleeding	489 (4·9%)	574 (5·7%)	0·85 (0·76–0·96)	0·0077
Vascular occlusion*	33 (0·3%)	48 (0·5%)	0·69 (0·44–1·07)	0·096
Multiorgan failure	209 (2·1%)	233 (2·3%)	0·90 (0·75–1·08)	0·25
Head injury	603 (6·0%)	621 (6·2%)	0·97 (0·87–1·08)	0·60
Other causes	129 (1·3%)	137 (1·4%)	0·94 (0·74–1·20)	0·63

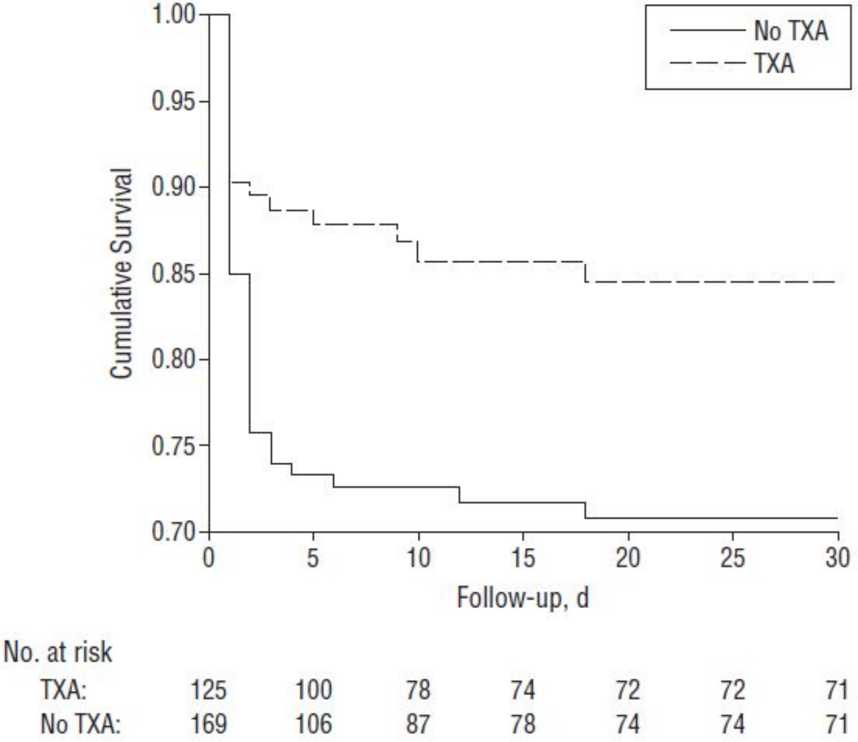
Data are number (%), unless otherwise indicated. RR=relative risk. *Includes myocardial infarction, stroke, and pulmonary embolism.

Table 2: Death by cause

TXA

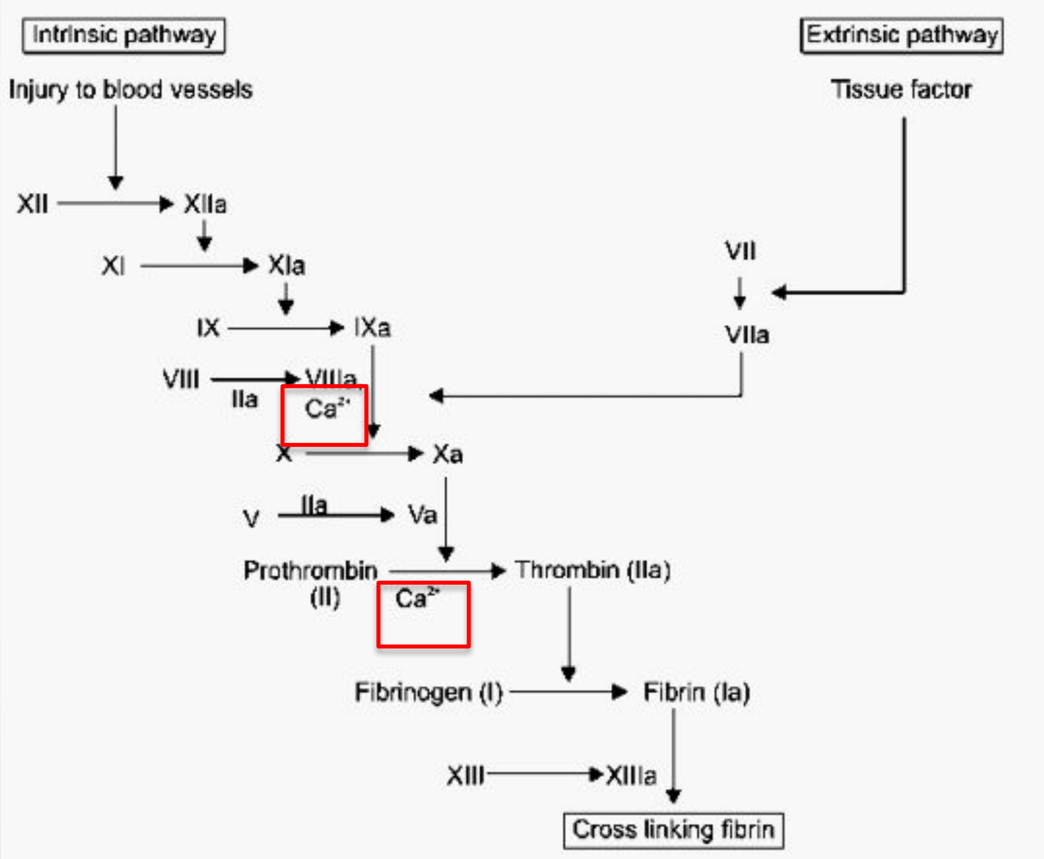


1.00
0.95
0.90
0.85
0.80
0.75
0.70
Cumulative Survival
0
5
10
15
20
25
30
Follow-up, d
No TXA
TXA
No. at risk
TXA: 293 220 172 159 155 152 148
No TXA: 603 351 269 246 231 226 218

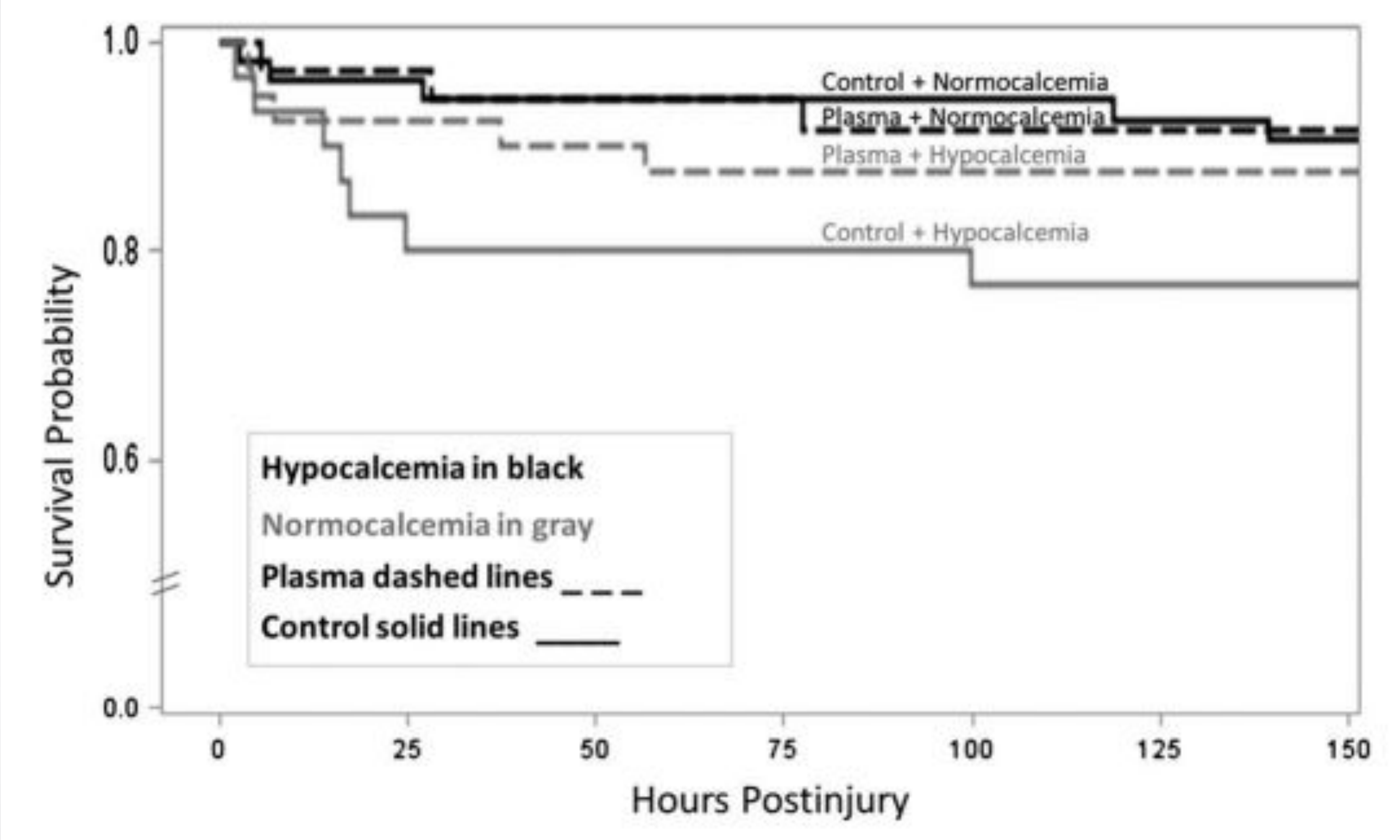


1.00
0.95
0.90
0.85
0.80
0.75
0.70
Cumulative Survival
0
5
10
15
20
25
30
Follow-up, d
No TXA
TXA
No. at risk
TXA: 125 100 78 74 72 72 71
No TXA: 169 106 87 78 74 74 71

Calcium



Intrinsic pathway
Injury to blood vessels
XII
XIIa
XI
XIa
IX
IXa
VIII
VIIIa
IIa
Ca2+
X
Xa
V
IIa
Va
Prothrombin (II)
Ca2+
Thrombin (IIa)
Fibrinogen (I)
Fibrin (Ia)
XIII
XIIIa
Cross linking fibrin
Extrinsic pathway
Tissue factor
VII
VIIa



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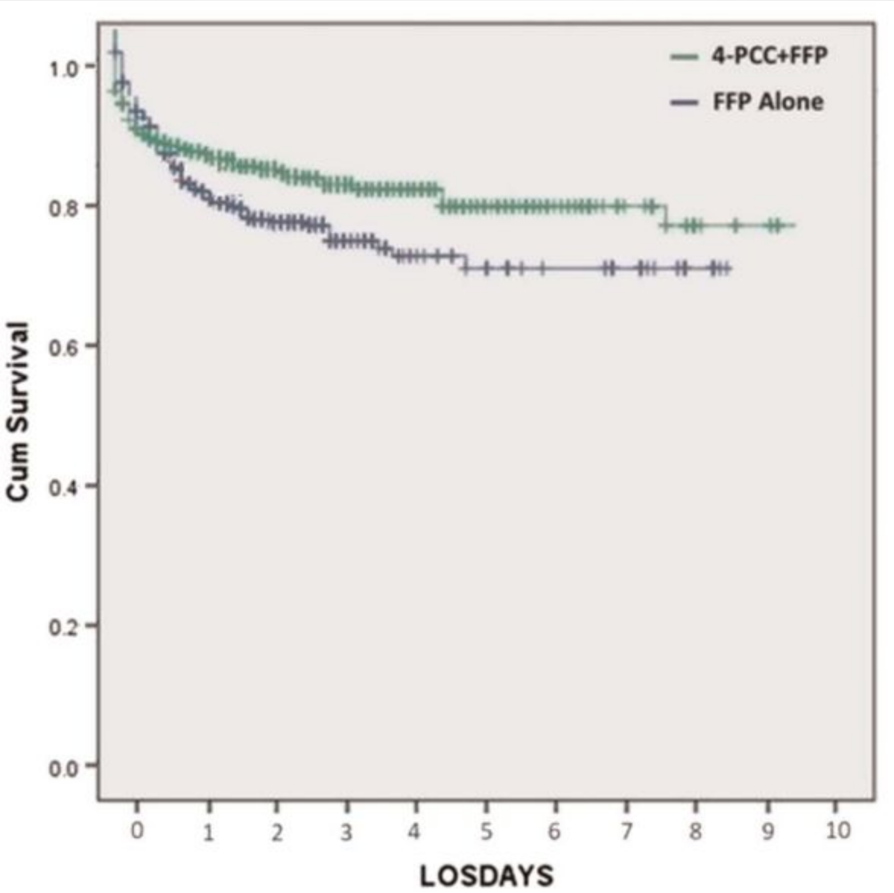
PCC



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Objectives

1. What is massive transfusion?
2. Who needs it?
3. Composition of modern massive resuscitation