Blood Preparedness Mass Casualty Events

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Lecture Outline

- **Optimal Trauma Care – Can it be Applied to Mass Casualties?**
- Trauma - Zero Preventable Deaths
- Time is the Enemy
- Interventions critical to reducing the rate of preventable deaths
  - Life-saving interventions
  - Blood transfusions
- Blood Failure
- Blood Supply in United States
  - Evaluations of Blood Preparedness for Mass Casualty Events – Focus on Rand Report
  - Where does the surge buffer reside?
  - Is it All Abut RBCs?
- Hospital Readiness
- Do We Need to Think and Practice Differently?
  - Can the "zero preventable deaths" strategies and thought processes apply to mass casualties?

Prehospital hemostatic resuscitation to achieve zero preventable deaths after traumatic injury

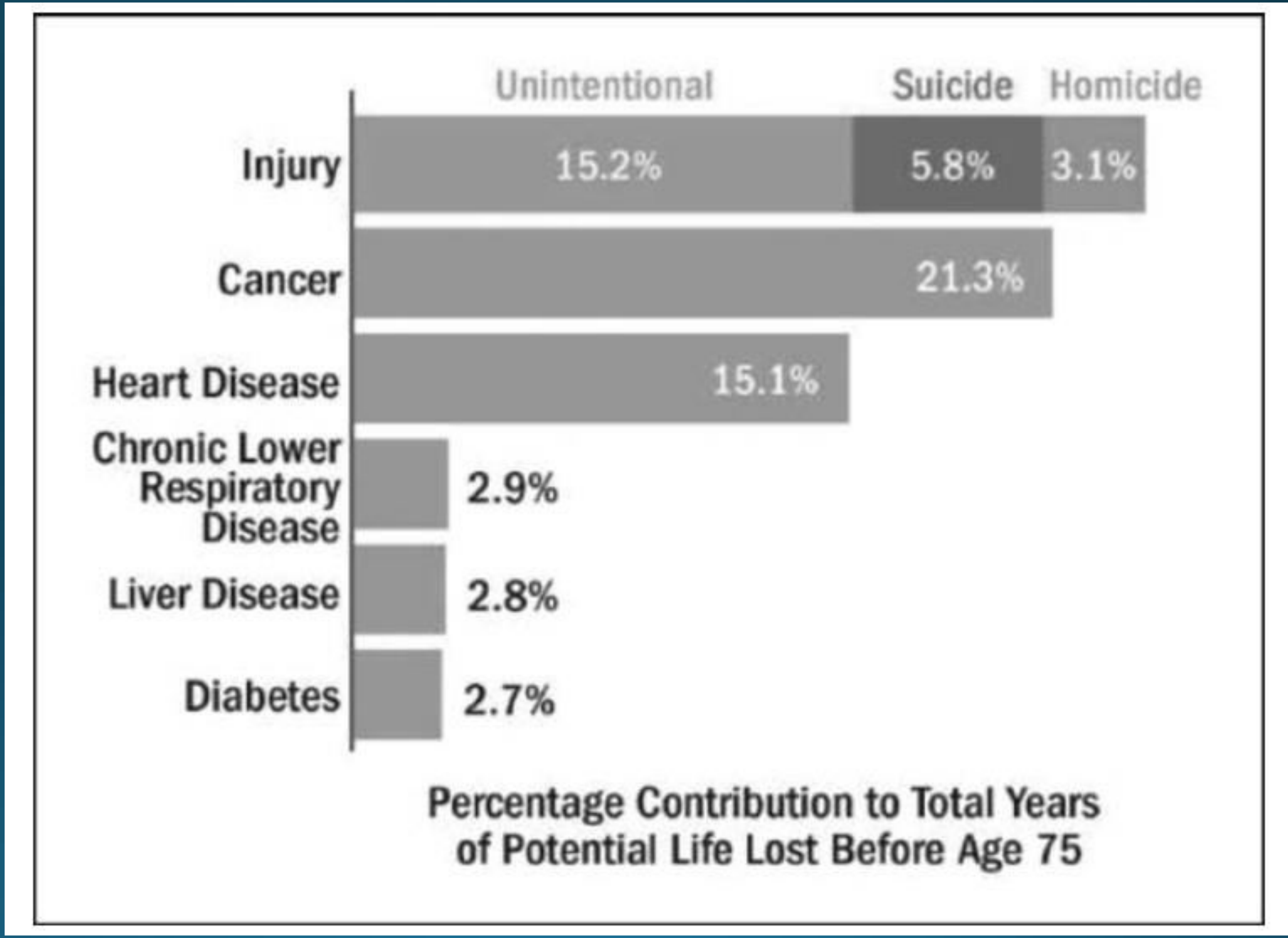
Philip C. Spinella[a,b] *and Andrew P. Cap*[b]

Curr Opin Hematol 2017; 24:529-535

In 2010 there were 5.1 million trauma-related deaths worldwide. This represents nearly 10% of all deaths. In the United States, trauma is the third leading cause of death when considering all age groups and is the leading cause of death for people 1–46 years of age.

Spinella and Cap – Curr Opin Hematol 2017; 24:529-535

Injury accounts for the highest percentage of years of potential life lost before the age of 75 years, compared with all other conditions, including cancer and heart disease – 24.1%



Zero Preventable Deaths

- **Spinella and Cap – Curr Opin Hematol 2017; 24:529-535**
- Preventable deaths after traumatic injury:

  "casualties whose lives could have been saved by appropriate and timely medical care, regardless of tactical, logistical, or environmental issues"

Spinella and Cap – Curr Opin Hematol 2017; 24:529-535

Table 1. Military and civilian deaths after traumatic injury

	Military data	Civilian data
Preventable deaths (pre and in-hospital) (%)	27.5[a]	20[b]
Deaths that occur prehospital (%)	90[c]	
Prehospital preventable deaths after traumatic injury (%)	25[c]	29[d]
Prehospital preventable hemorrhagic deaths after traumatic injury (%)	90[c]	64[d]
Deaths that occur in-hospital (%)	10[e]	
In-hospital preventable deaths after traumatic injury (%)	50[e]	
In-hospital preventable hemorrhagic deaths after traumatic injury (%)	80[e]	

The military data shows that 90% of trauma-related deaths occur in the prehospital setting. Military and civilian data show that the rate of preventable deaths after traumatic injury ranges from 20-27.5%, and prehospital preventable deaths due to hemorrhage range between 64% and 90%.

Zero Preventable Deaths

- **Spinella and Cap – Curr Opin Hematol 2017; 24:529-535**
- **Mathematics Fun!**
- 90% of trauma-related deaths – Prehospital - ~130,000
  - 29% of civilian Prehospital deaths – Preventable - ~38,000
  - 64% of preventable Prehospital deaths – Hemorrhage - ~25,000
- US - Prehospital + in-hospital deaths - ~30 000 hemorrhage-related deaths per year - Preventable after injury
  - Vast majority – Preventable hemorrhage-related deaths – Prehospital
- **30,000 people bleed to death every year in the US after trauma and these people SHOULD NOT DIE if trauma care was maximally effective**
- **25,000 of the 30,000 die (of a preventable death) BEFORE they get to the hospital!**
- **This is a treatment gap that must be filled – This includes filling the same gap for mass casualty incidents!**

What Is The Problem?

Time is the Enemy!

Time is the enemy: Mortality in trauma patients with hemorrhage from torso injury occurs long before the "golden hour"

A.Q. Alarhayem [a], J.G. Myers [a], D. Dent [a], L. Liao [a], M. Muir [a], D. Mueller [a], S. Nicholson [a], R. Cestero [a], M.C. Johnson [a], R. Stewart [a], Grant O'Keefe [b], B.J. Eastridge [a, *]

[a] *The University of Texas Health Science Center at San Antonio, Department of Surgery, Division of Trauma, Critical Care, and Acute Care Surgery, United States*
[b] *University of Washington, Department of Surgery, Division of Trauma and Acute Care Surgery, United States*

The American Journal of Surgery 212 (2016) 1101–1105

"Torso AIS and prehospital time were noted to be strong independent predictors of patient mortality in all population strata of the analysis (P < 0.05). The data demonstrated a profound incremental increase in mortality in the early time course after injury associated with torso AIS 4."

"In patients with high-grade torso injury, AIS grades 4, the degree of anatomic disruption is associated with significant hemorrhage. In our study, a precipitous rise in patient mortality was exhibited in this high-grade injury group at prehospital times <30 min."

Alarhayem et al – Am J Surg 2016; 212:1101-1105

Caregivers have less than 30 minutes to have a positive impact on preventable death rates in patients with severe torso injury!

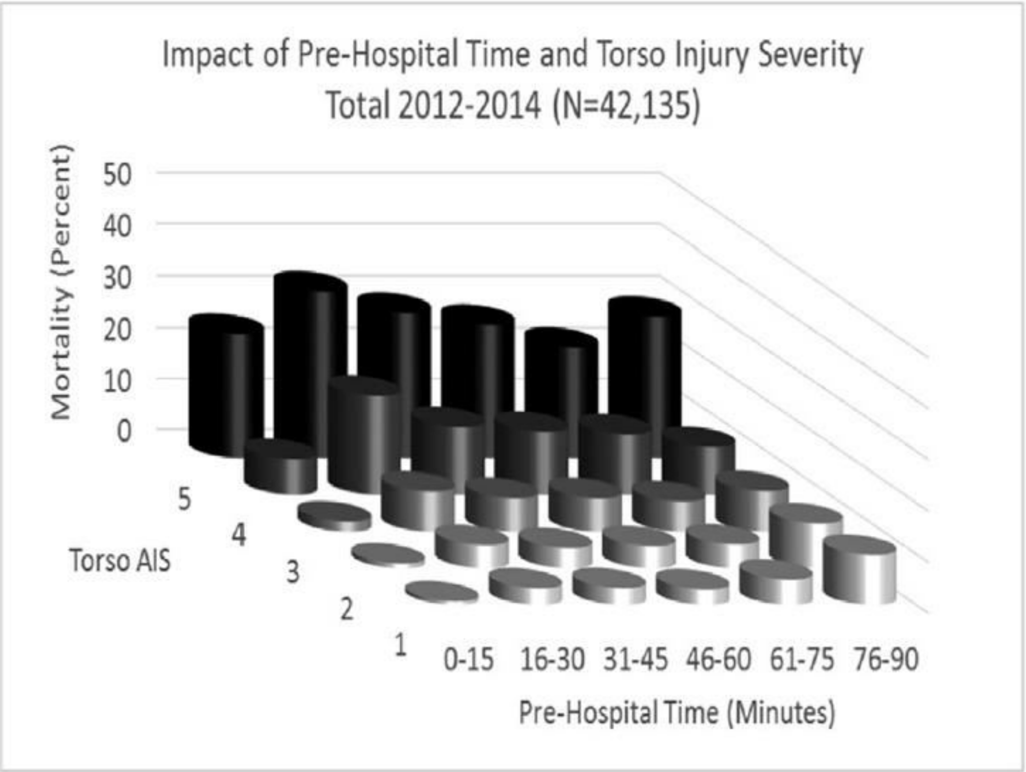


Fig. 1. Mortality Impact of prehospital time and torso injury severity for composite population 2012–2014 (N = 42,135).

“ If we going to have a significant impact on preventable trauma-related deaths, then improvement of care in the first minutes after severe injury is absolutely essential. ”

This should be pursued whether we are dealing with single patients or mass casualty events – Ideally we should have the capability to provide equal standards of care in both settings!

Personal Opinion

What Can Be Done?

Early Interventions!

Remote damage control resuscitation and the Solstrand Conference: defining the need, the language, and a way forward

Robert T. Gerhardt, Geir Strandenes, Andrew P. Cap, Francisco J. Rentas, Elon Glassberg, Jeff Mott, Michael A. Dubick, and Philip C. Spinella for the THOR Network and RemTORN Study Groups

- Transfusion 2013; 53:9S-16S
- Causes - Potentially survivable combat death
  - Underperformance of Life-Saving Interventions (LSI) when required
  - Combination of uncontrolled major hemorrhage (UMH) and delayed evacuation to surgical intervention

An analysis of prehospital deaths: Who can we save?

James S. Davis, MD, Shevonne S. Satahoo, MD, Frank K. Butler, MD, Harrison Dermer, Daniel Naranjo, MD, Katherina Julien, Robert M. Van Haren, MD, MSPH, Nicholas Namias, MD, MBA, Lorne H. Blackbourne, MD, *and* **Carl I. Schulman, MD, PhD, MSPH,** *Miami, Florida*

J Trauma Acute Care Surg 2014; 77:213-218

Prehospital tourniquet use is **critically important lifesaving measure** advocated for by TCCC for the **US Military**. Prior to the introduction of TCCC concepts, US military personnel were taught to use tourniquets only as a last resort to control external hemorrhage. A **study of 2,600 combat fatalities in Vietnam** documented a **7.4% incidence** of **death from extremity hemorrhage**. Exsanguination from extremity hemorrhage was the **leading cause** of **preventable death in Vietnam**. The high incidence of death from extremity hemorrhage persisted into more recent conflicts. A **study of 982 fatalities from the early years of the wars in Afghanistan and Iraq** found that the **percentage** of **combat fatalities** that **died of extremity hemorrhage** was essentially unchanged at **7.8%**. **Widespread use of tourniquets by US forces began in 2005**. After tourniquet implementation, death from extremity hemorrhage became increasingly uncommon. The **"Death on the Battlefield" study of 4,596 US combat fatalities from 2001 to 2011** found that **preventable deaths from extremity hemorrhage** had **decreased to** 2.6% of the total, a reduction of 66% from the "Kelly Study" published in 2008. The **number of lives saved** from **widespread tourniquet use** has been estimated to be **between 1,000 and 2,000**.

Zero Preventable Prehospital Deaths !
Is This An Achievable Goal?

Yes….If you are an Army Ranger!

Eliminating Preventable Death on the Battlefield

Russ S. Kotwal, MD, MPH; Harold R. Montgomery, NREMT; Bari M. Kotwal, MS; Howard R. Champion, FRCS; Frank K. Butler Jr, MD; Robert L. Mabry, MD; Jeffrey S. Cain, MD; Lorne H. Blackbourne, MD; Kathy K. Mechler, MS, RN; John B. Holcomb, MD

Arch Surg 2011; 146:1350-1358

This study was an analysis of battle injury data for the 75th Ranger Regiment, US Army Special Operations Command in Afghanistan and Iraq from October 1, 2001, through March 31, 2010. There were 419 casualties during 7 years of continuous combat in Iraq and 8.5 years in Afghanistan. The **rates of 10.7% killed in action and 1.7% who died of wounds were lower than the Department of Defense rates of 16.4% and 5.8%**, respectively, for the larger US military population (*P*=.04 and *P*=.02, respectively). Of **32 fatalities**, none died of wounds from infection, **none were potentially survivable through additional prehospital medical intervention. There were no preventable deaths due to extremity hemorrhage exsanguination.**

Table 3. Hemorrhage Control Interventions Administered by 75th Ranger Regiment Personnel by Provider Level During Care Under Fire and Tactical Field Care Phases of Tactical Combat Casualty Care Between October 1, 2001, and March 31, 2010[a]

	Care Provider Level, No.				
Intervention	RFR	Nonmedic EMT	Medic	Medical Officer	Total, No.
Pressure dressing[b]	33	16	136	21	**206**
Gauze dressing	28	16	121	23	**188**
Tourniquet[c]	27	10	49	3	**89**
Hemostatic dressing[d]	3	1	26	7	**37**
Total	**91**	**43**	**332**	**54**	**520**

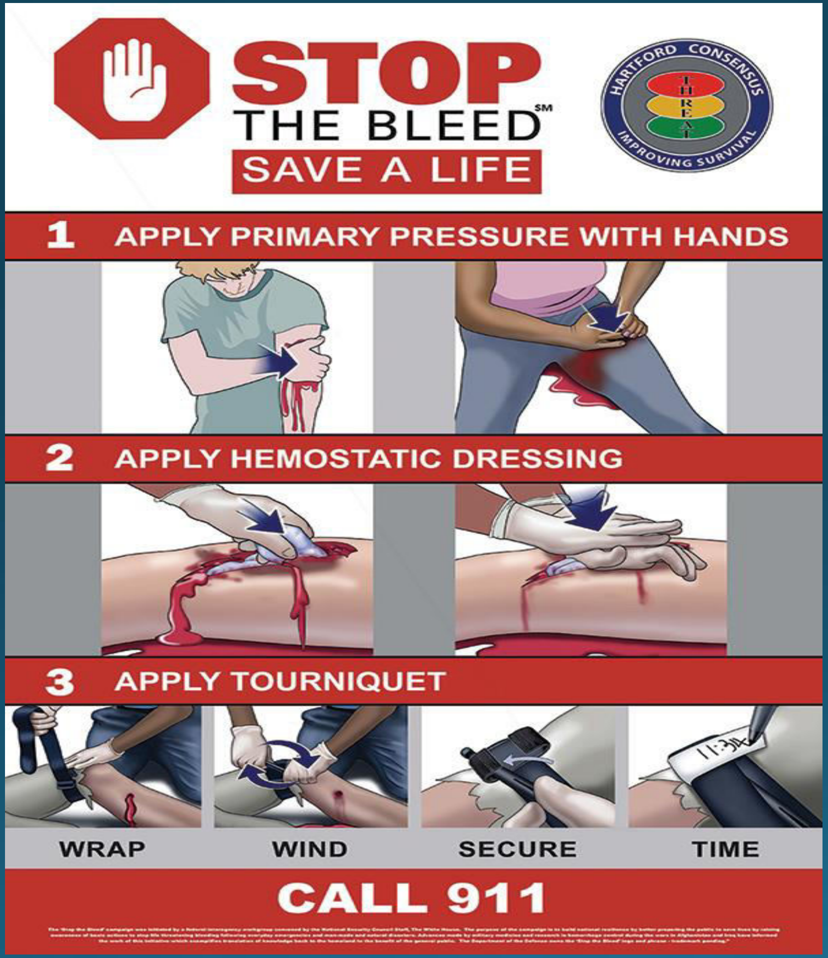
Abbreviations: EMT, emergency medical technician; RFR, Ranger First Responder.
[a] Nonmedical personnel provided 26% (134/520) of all hemorrhage control interventions and 42% (37/89) of all tourniquets.
[b] Primarily Emergency Trauma Dressings (North American Rescue, LLC, Greer, South Carolina).
[c] Primarily Combat Application Tourniquets (Composite Resources, Rock Hill, South Carolina).
[d] Primarily HemCon bandages (HemCon Medical Technologies, Inc, Portland, Oregon) and Combat Gauze (Z-Medica Corp, Wallingford, Connecticut).

Arch Surg 2011; 146:1350-1358

Non-medical personnel delivered 26% of all hemorrhage control interventions and 42% of tourniquets! Key contribution to no prehospital deaths from extremity hemorrhage.

Life Saving Interventions

We must educate, train, and empower non-medical "pre" first responders to act and administer life-saving interventions after trauma-related injuries, this issue would seem to be amplified and an even more compelling need in mass casualty situations



This concept is just as, if not more important, early aggressive transfusion therapy in trauma patients, including mass casualty events!

What About Blood Transfusions?

Are Prehospital Blood Transfusions Beneficial?

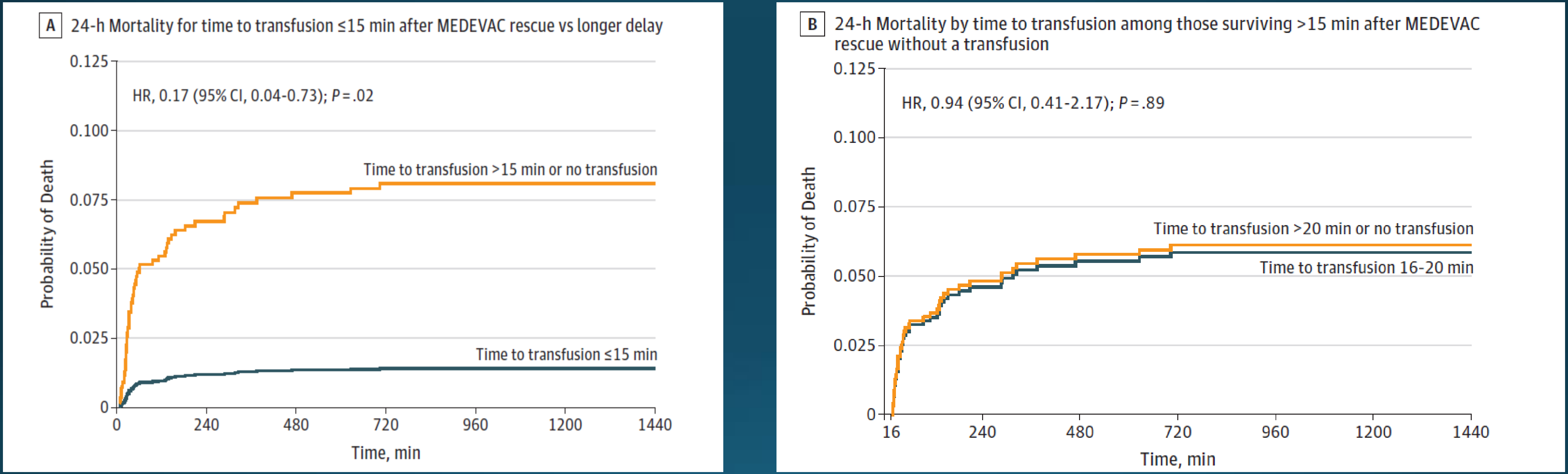
JAMA | Original Investigation

Association of Prehospital Blood Product Transfusion During Medical Evacuation of Combat Casualties in Afghanistan With Acute and 30-Day Survival

Stacy A. Shackelford, MD; Deborah J. del Junco, PhD; Nicole Powell-Dunford, MD; Edward L. Mazuchowski, MD, PhD; Jeffrey T. Howard, PhD; Russ S. Kotwal, MD, MPH; Jennifer Gurney, MD; Frank K. Butler Jr, MD; Kirby Gross, MD; Zsolt T. Stockinger, MD

JAMA. 2017;318(16):1581-1591.

Shackelford et al - JAMA 2017; 318:1581-1591



Maybe it is Not the Location but the Timing of Transfusions!

Do Very Early Transfusions Make Sense?

Blood Failure

Trauma victims having tissue injury and hemorrhagic shock are susceptible to hemorrhagic blood failure. Hemorrhagic blood failure arises when individuals reach a critical level of oxygen debt (shock). Hemorrhagic shock triggers a cascade of "dysfunction" involving the endothelium, platelets, and the coagulation system resulting in the blood failure syndrome. Blood failure is associated with dramatically increased mortality. This condition can develop very rapidly in severely injured individuals.

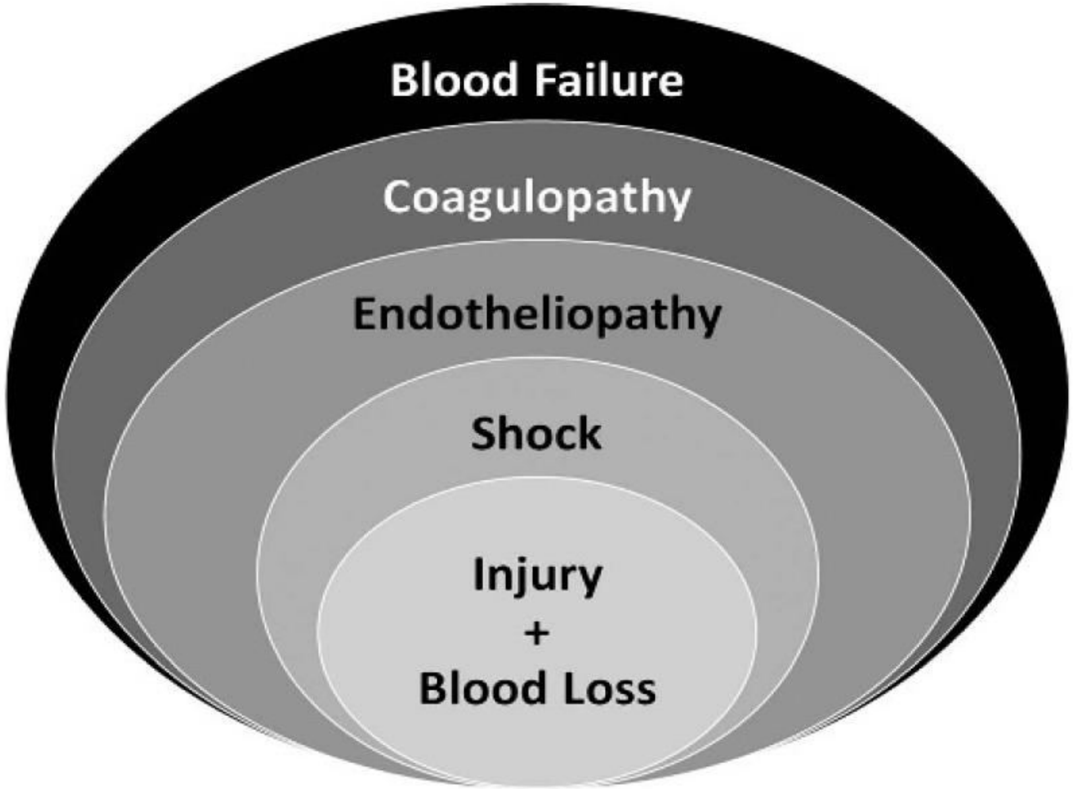
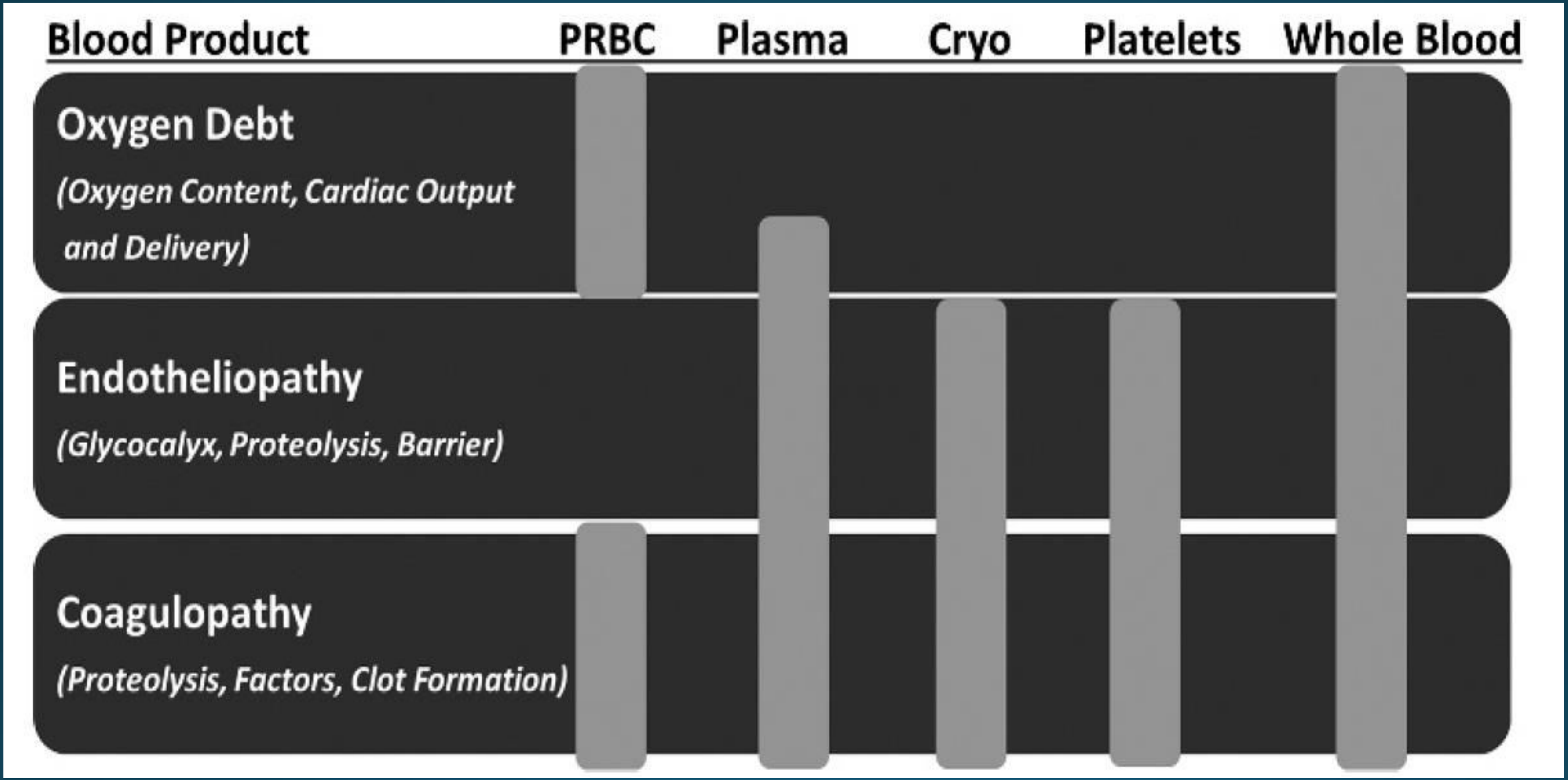


Figure 1. Schematic representing the components of hemorrhagic blood failure.

J Trauma Acute Care Surg 2017; 82:S41-S49



J Trauma Acute Care Surg 2017; 82:S41-S49

The treatment of hemorrhagic blood failure requires that its multiple components be address dealt with simultaneously as outlined in this figure. **This means that having adequate RBCs does not satisfactorily address the problem!**

Blood Supply

Toward a Sustainable Blood Supply in the United States

An Analysis of the Current System and Alternatives for the Future

Published by the RAND Corporation, Santa Monica, Calif.

Rand Analysis – Blood Supply

- Historically - Terrorist-related disasters - Not created immediate blood shortages
- United States - Not yet experienced - Critical shortage of blood components – Immediate aftermath - Mass casualty event
- Success attributed – U.S. blood component distribution system - Regional surpluses of blood components transported to locations of in need

Rand Analysis – Blood Supply

- Examples of U.S. events - More than 100 units of blood in the first 24 to 30 hours following the incident
  - 1981 collapse in Kansas City, Missouri,
  - 1989 airplane crash landing n Sioux City, Iowa
  - 1995 federal building bombing in Oklahoma City, Oklahoma
  - 1999 shooting at Columbine High School in Denver, Colorado
  - 2001 attacks in New York City, New York (9/11)
  - 2012 Sandy Hook shooting in Newtown, Connecticut
  - 2016 nightclub shooting in Orlando, Florida
- Events - Cities of various sizes   - Different times of the week - Different types of injuries
- Blood collections - Managed locally - Blood from outside sources not needed
- To Date - U.S. blood system – Robust enough - Effectively respond to disaster events

Blood Supply

- Resiliency in the blood supply – Critical - Surge demands - Public health emergencies
- Maintenance - Surplus capacity - Blood collection system – Integral - Meeting future emergency
- challenges
- 2015 NBCUS findings – Cost of maintaining surplus - Community-based blood collection centers
- Number of RBC units outdated - Community-based blood collection centers increased since 2011 but declined in hospitals
- Nontransfused units - More likely to expire at a blood collection center than a transfusing hospital
- Suggest - Transfusing facilities - Tightly managing blood component inventories
- Sufficient reserve of blood products - Context of declining demand – Unknown
- Lower hospital inventories – Less immediate availability of blood components during surges!!!!
  - **Is this a step backwards for optimal trauma care of a large number of casualties (Damage Control Resuscitation and Remote Damage Control Resuscitation)?**
- **The Rand Report and other simulations/analyses have focused on providing RBCs with conclusions/reassurance that we can move RBCs quickly and effectively to areas of need. This ignores the other crucial components necessary to treat blood failure, and, even if we focus on RBCs, moving RBCs from Blood Centers does not satisfy the crucial need for blood products as soon as possible after injury!**

A Deeper Dive

Blood Supply

Continued decline in blood collection and transfusion in the United States–2015

Katherine D. Ellingson,[1,2] *Mathew R. P. Sapiano,*[1,3] *Kathryn A. Haass,*[1] *Alexandra A. Savinkina,*[1,4] *Misha L. Baker,*[1,5] *Koo-Whang Chung,*[1] *Richard A. Henry,*[6] *James J. Berger,*[6] *Matthew J. Kuehnert,*[1] *and Sridhar V. Basavaraju*[1]

TRANSFUSION 2017;57;1588–1598

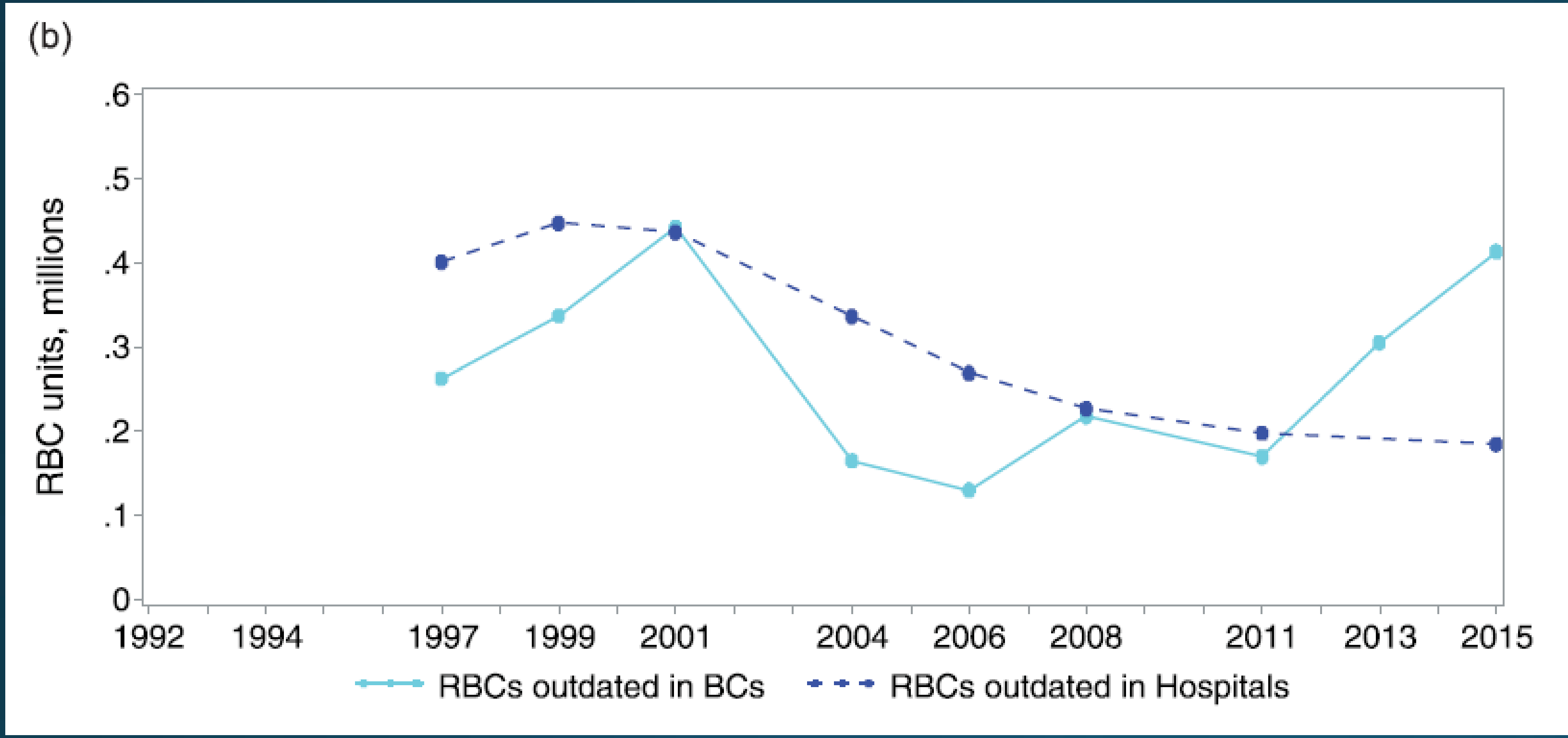
TABLE 1. Estimated numbers of whole blood and RBC units collected, transfused, and outdated in 2015 (expressed in thousands)

	Blood centers	Hospitals	Combined totals	95% CI	2013 Totals*	% Change 2015-2013
Collections						
Whole blood units						
Allogeneic, nondirected	10,220	529	10,748	10,176-11,321	12,109	−11.2
Autologous	18	7	25	19-31	61	−59.0
Directed	11	10	21	14-28	24	−12.3
Apheresis RBC units†	1,773	24	1,797	1,551-2,043	2,043	−12.1
Total supply	12,022	569	12,591	11,985-13,197	14,237	−11.6
Rejected on testing	46	7	53	42-63	98§	
Rejected for other reasons‡	480	30	510	457-562	744§	
Total available supply	11,496	532	12,028	11,454-12,603	13,395	−10.2
Transfusions						
Allogeneic, nondirected		11,264		10,868-11,659	13,093	−14.0
Autologous		20		8-32	44	−54.2
Directed		66		35-96	43	52.3
Total transfusions		11,349		10,952-11,747	13,180	−13.9
Outdated whole blood or RBCs	414	186	600	542-658		

TABLE 2. Estimated number of platelets, plasma, and cryoprecipitate units distributed, transfused, and outdated in 2015 (expressed in thousands)

Variable	Blood centers	Hospitals	Combined totals	95% CI	2013 Totals*	% Change 2015-2013
Distributed						
Apheresis platelets	2034	200	2234	2040-2429	2318	−3.6
Whole-blood–derived PLTs†	189	13	202	146-257	130	55.0
Total platelets	2223	213	2436	2230-2642	2448	−0.5
Total plasma	3450	264	3714	3306-4121	4338	−14.4
Cryoprecipitate‡	1694	163	1857	1605-2109	978	89.9
Blood center outdates§	217	25	242	211-273	239	1.2
Transfused						
Apheresis platelets		1807		1670-1943	2137	−15.4
Whole-blood–derived PLTs†		171		84-258	128	33.7
Total platelets (includes directed units)		1983		1816-2151	2281	−13.1
Total plasma		2727		2594-2859	3624	−24.8
Cryoprecipitate‡		1167		1021-1314	1095	6.6
Hospital outdates‖		426		392-461	395	7.9

TRANSFUSION 2017;57;1588–1598



The "buffer" of blood components resides in blood centers and NOT next to the patients in health care facilities!

TRANSFUSION 2017;57;1588–1598

Major Issue

Blood Management ≠ Emergency Blood Preparedness

2008 Inventory Goals

We tried to maintain approximately 2000 RBCs in inventory at all times to meet demands and have a buffer if we had an MCE or a supply chain issue.

Red Blood Cell Inventory Levels Attachment I

Product Inventory Levels	Blood Type	Maximum	Optimum	Minimum (replenish over next several days)	Panic (replenish immediately)
RBC	O+	850	650	460	400
	A+	820	650	460	400
	B+	220	170	110	90
	AB+	NA	NA	NA	NA
	O-	230	190	140	120
	A-	220	180	140	120
	B-	36	30	20	10
	AB-	NA	NA	NA	NA
	Total	2,376	1,870	1330	1140

Patient blood management and adoption of more conservative transfusion practices have resulted in significant changes at our facility and we have had to adjust our standing inventory goals – The in house "buffer" to address mass casualties has decreased!

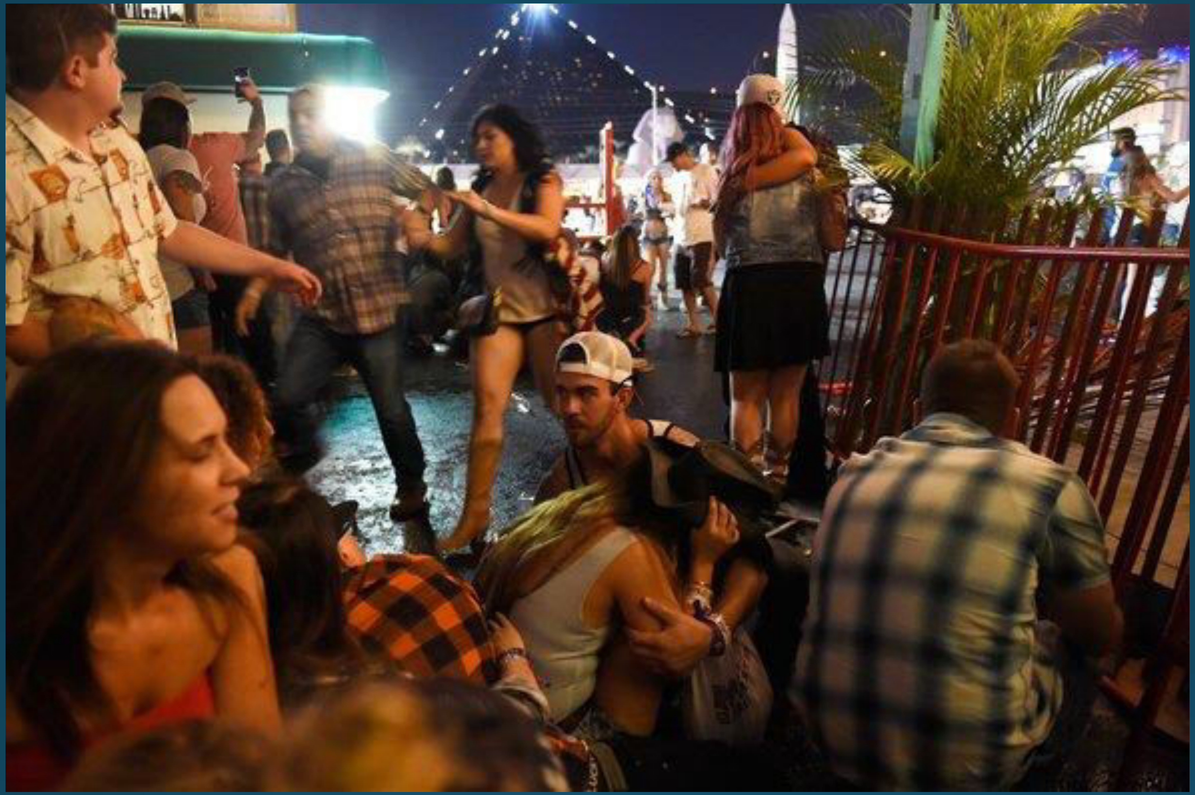
RBCs - New Optimum Levels as of October 1st, 2016

ABO	Available	Optimum	Minimum	DS to Call	RBC's From ARC Today	From ARC tomorrow
O pos	269	375	282	X	40	
A pos	220	280	210	X	20	
B pos	57	69	52	X		
AB pos	25	20	15	X		
O neg	87	107	81	X	10	
A neg	76	71	53			
B neg	17	17	12	X		
AB neg	10	6	5			
Total	761	945	710			

~50,000 RBCs Transfused in 2008 and ~28,000 RBCs Transfused in 2016

Mass Casualty Events

Mass Shootings in the U.S.



Oct. 1, 2017. Las Vegas

A gunman opened fire on a crowd of more than 22,000 at a concert in Las Vegas, killing 58 people and injuring about 500, the authorities said, making it one of the deadliest mass shootings ever in the United States.

New York Times October 2, 2017

Mass Casualty Events

- Critical Question – Are Transfusion Medicine services able to support resuscitation efforts in a manner that supports the current standard of practice for severely injured patients when there are multiple victims?
- The goal of Zero Preventable Deaths should be the same regardless of the number of victims!

Managing the surge in demand for blood following mass casualty events: Early automatic restocking may preserve red cell supply

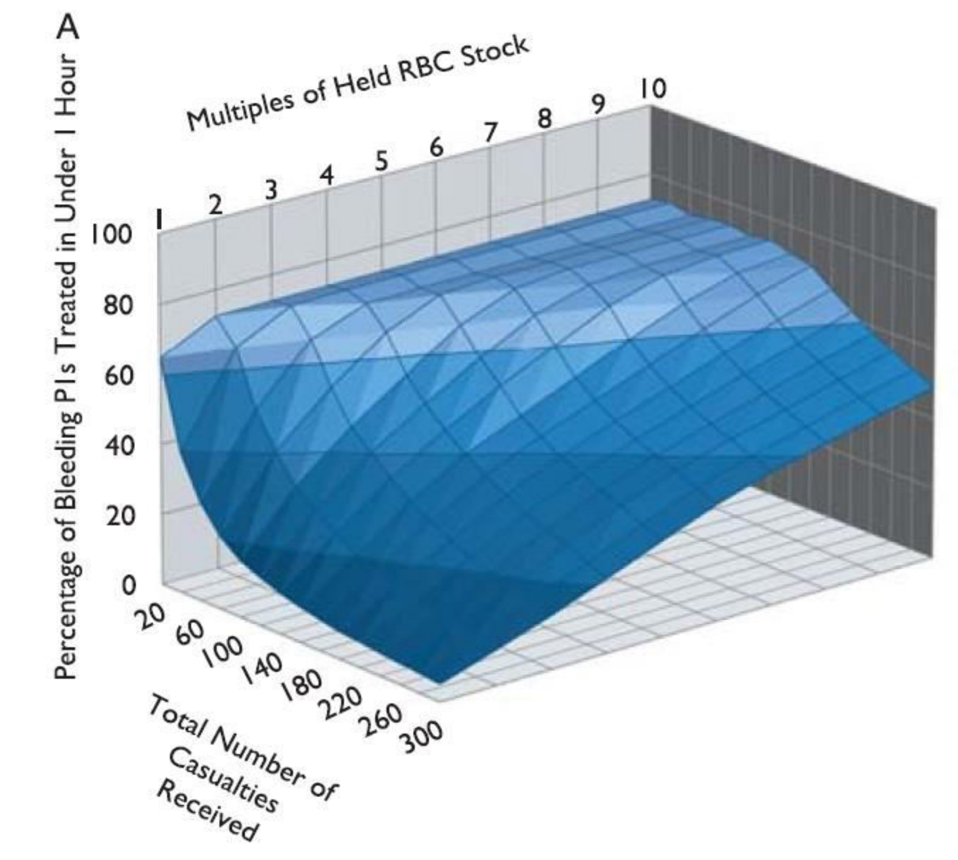
Simon Glasgow, MD, Christos Vasilakis, MSc, PhD, Zane Perkins, MD, Susan Brundage, MD, Nigel Tai, MS, MD, *and* Karim Brohi, MD, *London, United Kingdom*

J Trauma Acute Care Surg 2016;81: 50–57

TABLE 2. Volume of Each Type of Blood Group Held On-Shelf at the Start of the Simulation for Each Multiple of the Basic Inventory State (Shown as Units of RBC)

Aim 1 Experimental Model Inputs

	Multiples of Basic Inventory Stock Level									
Blood Group	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Type O RBC	100	200	300	400	500	600	700	800	900	1,000
Type A RBC	75	150	225	300	375	450	525	600	675	750
Type B RBC	25	50	75	100	125	150	175	200	225	250
Type AB RBC	10	20	30	40	50	60	70	80	90	100
Total RBC Stock	210	320	630	840	1,050	1,260	1,470	1,680	1,890	2,100



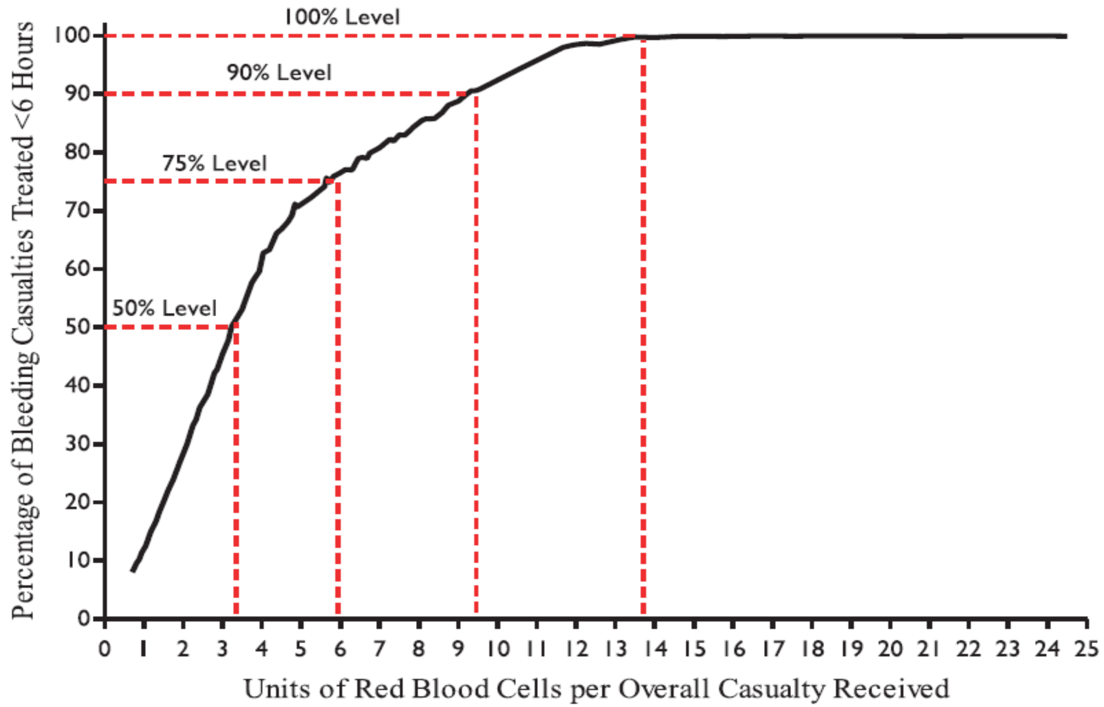


Figure 3. Relationship between units of RBC held per casualty received and the percentage of all bleeding casualties treated within 6 hours.

Fun With Numbers - Mayo

- Average daily platelet use – 27
- Average RBC use – 75
  - Average O positive RBC use – 30
  - Average O negative RBC use - 8
- October 2, 2017 – 55 platelets and 705 RBCs
  - 245 O positive RBCs
  - 79 O negative RBCs
- Inventory left over for MCE
  - 28 platelets
  - 215 O positive RBCs
  - 71 O negative RBCs

Fun With Numbers

- 6:6:1 emergency resuscitation - Dose
- 215 ÷ 6 = 35 "doses" of O positive RBCs
- 71 ÷ 6 = ~12 "doses" of O negative RBCs
- 28 "doses" of platelets
- 20 casualties – 2 doses (10 men and 10 women)
  - 120 group O positive RBCs + 12 platelets - Men
  - 120 group O negative RBCs + 12 platelets – Women
  - 95 group O positive RBCs remaining
  - Shortage – 49 group O negative RBCs
  - 4 platelets remaining

To Decrease **Preventable Deaths**, Trauma Victims Need Balanced Resuscitation **EARLY**! This Means Plasma and Platelets as Well as RBCs. Therefore, Analysis and Simulations of RBC Supplies and Mobilization from Blood Centers Miss the Mark!!!

RBCs = Plasma = Platelets in Importance

ALL Need to be Transfused **EARLY** (Platelet Availability Drives the System of Readiness NOT RBCs!).

Pre-Hospital Trauma Care

- Spinella and Cap – Curr Opin Hematol 2017; 24:529-535
- **Low titer group O Whole Blood**
- **Cold-stored platelets**
- **Tranexamic acid**
- Lyophilized plasma
- Fibrinogen concentrates

Balanced Resuscitation Efforts

We Have Been “Pushing The Envelope” at Mayo Clinic

How we provide thawed plasma for trauma patients

James R. Stubbs,[1] Martin D. Zielinski,[2] Kathleen S. Berns,[3] Karafa S. Badjie,[1] Craig D. Tauscher,[1] Scott A. Hammel,[1] Scott P. Zietlow,[2] and Donald Jenkins[2]

Transfusion 2015; 55:1830-1837

Group A Thawed Plasma Program Started in 2008

The state of the science of whole blood: lessons learned at Mayo Clinic

James R. Stubbs,[1] Martin D. Zielinski,[2] and Donald Jenkins[2]

Transfusion 2016; 56:S173-S181

Whole Blood Program Started in 2015

Cold platelets for trauma-associated bleeding: regulatory approval, accreditation approval, and practice implementation—just the “tip of the iceberg”

James R. Stubbs,[1] Sheryl A. Tran,[2] Richard L. Emery,[1] Scott A. Hammel,[1] De Anna L. Haugen,[3] Martin D. Zielinski,[4] Scott P. Zietlow,[4] and Donald Jenkins[4]

Transfusion 2017; 57:2836-2844

Cold Platelet Program Started in 2015

THE FEASIBILITY OF A WARM FRESH WHOLE BLOOD DONATION PROGRAM IN A CIVILIAN HEALTH SYSTEM

Joy D. Hughes MD, Matthew C Hernandez MD, Mariela Rivera MD, FACS, Mark Sawyer, MD, FACS, Justin D. Kreuter, James R. Stubbs, MD, Martin D. Zielinski, MD, FACS*

In Preparation

Can These Approaches Be Utilized For Civilian Trauma When There Are Mass Casualties?

My Thoughts

- Current Blood Donor Availability/Management + Blood Inventory Management + Patient Blood Management + Financial Considerations:
- I feel that some of these important approaches to trauma care are not going to be feasible for a mass casualty event – What is reasonable for a few will not work for a large number of simultaneously injured victims
- You can't stockpile Whole Blood (storage 14 days to maybe 35 days) and Cold Platelets in hospitals to provide early balanced resuscitation at hospitals or prehospital just in case multiple casualties hit the door (stockpiling at blood centers will also be not feasible and too late!)
- You can give TXA and we should/must teach more people how to "Stop The Bleed!"
- Challenge – How do we achieve a similar standard of care for mass casualties as we expect for individual trauma victims?

My Thoughts

- We need to achieve balanced resuscitation with products that can be stockpiled for long time periods
  - Freeze Dried Plasma – We need FDA approval
  - Frozen or Lyophilized Platelets
  - Fibrinogen Concentrates
  - Cryoprecipitate Preparations - Stored long-term and rapidly provided in times of need (fibrinogen + vWF + Factor XIII)
  - Factor Concentrates – PCCs etc.
- We must not accept – A "dumbed down" standard of care when we encounter mass casualties
- Creative and Innovative Thinking – Achieve
  - Zero Preventable Deaths – Mass Casualty Settings
  - Our Current State (even the reassurances that RBCs can be moved quickly from blood centers regionally and nationally) – Is far from achieving this goal

Questions?

Live Saving Interventions

- United States Department of Defense - Tactical Combat Casualty Care (TCCC)
- Important lifesaving intervention - Pre-hospital tourniquets
- Vietnam – Exsanguination from extremity hemorrhage – Leading cause of preventable death
- Field medical personnel - Tourniquets - Last resort to control external hemorrhage
- Vietnam Study of 2,600 combat fatalities
  - Extremity hemorrhage - 7.4% of deaths
- Early years - Afghanistan and Iraq - Study of 982 fatalities
  - Extremity hemorrhage - 7.8% of deaths

Live Saving Interventions

- Tourniquets widespread - US forces in 2005
- Extremity hemorrhage death – Less common
- Study - 4,596 US combat fatalities from 2001 to 2011
  - Incidence of deaths - Extremity hemorrhage – 2.6% of deaths
  - 66% reduction from previously reported incidence in Afghanistan and Iraq
- Number of lives saved from widespread tourniquet use
  - Estimated to be between 1,000 and 2,000.

Zero potentially survivable deaths occurring in the prehospital setting!

Eliminating Preventable Death on the Battlefield

Russ S. Kotwal, MD, MPH; Harold R. Montgomery, NREMT; Bari M. Kotwal, MS; Howard R. Champion, FRCS; Frank K. Butler Jr, MD; Robert L. Mabry, MD; Jeffrey S. Cain, MD; Lorne H. Blackbourne, MD; Kathy K. Mechler, MS, RN; John B. Holcomb, MD

Objective: To evaluate battlefield survival in a novel command-directed casualty response system that comprehensively integrates Tactical Combat Casualty Care guidelines and a prehospital trauma registry.

Design: Analysis of battle injury data collected during combat deployments.

Setting: Afghanistan and Iraq from October 1, 2001, through March 31, 2010.

Patients: Casualties from the 75th Ranger Regiment, US Army Special Operations Command.

Main Outcome Measures: Casualties were scrutinized for preventable adverse outcomes and opportunities to improve care. Comparisons were made with Department of Defense casualty data for the military as a whole.

Results: A total of 419 battle injury casualties were incurred during 7 years of continuous combat in Iraq and 8.5 years in Afghanistan. Despite higher casualty severity indicated by return-to-duty rates, the regiment's rates of 10.7% killed in action and 1.7% who died of wounds were lower than the Department of Defense rates of 16.4% and 5.8%, respectively, for the larger US military population ($P = .04$ and $P = .02$, respectively). Of 32 fatalities incurred by the regiment, none died of wounds from infection, none were potentially survivable through additional prehospital medical intervention, and 1 was potentially survivable in the hospital setting. Substantial prehospital care was provided by nonmedical personnel.

Conclusions: A command-directed casualty response system that trains all personnel in Tactical Combat Casualty Care and receives continuous feedback from prehospital trauma registry data facilitated Tactical Combat Casualty Care performance improvements centered on clinical outcomes that resulted in unprecedented reduction of killed-in-action deaths, casualties who died of wounds, and preventable combat death. This data-driven approach is the model for improving prehospital trauma care and casualty outcomes on the battlefield and has considerable implications for civilian trauma systems.

Arch Surg. 2011;146(12):1350-1358. Published online August 15, 2011. doi:10.1001/archsurg.2011.213

Prehospital Transfusions

PREHOSPITAL BLOOD PRODUCT RESUSCITATION FOR TRAUMA: A SYSTEMATIC REVIEW

Iain M. Smith,[*†‡] Robert H. James,[§||¶] Janine Dretzke,[***] and Mark J. Midwinter[*†]

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SHOCK, Vol. 46, No. 1, pp. 3–16, 2016

No prospective comparative or randomized studies were identified. Sixteen case series and 11 comparative studies were included in the review. Seven studies included mixed populations of trauma and nontrauma patients. Twenty-five of 27 studies provided only very low quality evidence. No association between PHBP and survival was found (OR for mortality: 1.29, 95% CI: 0.84–1.96, P = 0.24). A single study showed improved survival in the first 24 h. No consistent physiological or biochemical benefit was identified, nor was there evidence of reduced in-hospital transfusion requirements. Transfusion reactions were rare, suggesting the short-term safety of PHBP administration.

Prehospital Transfusions

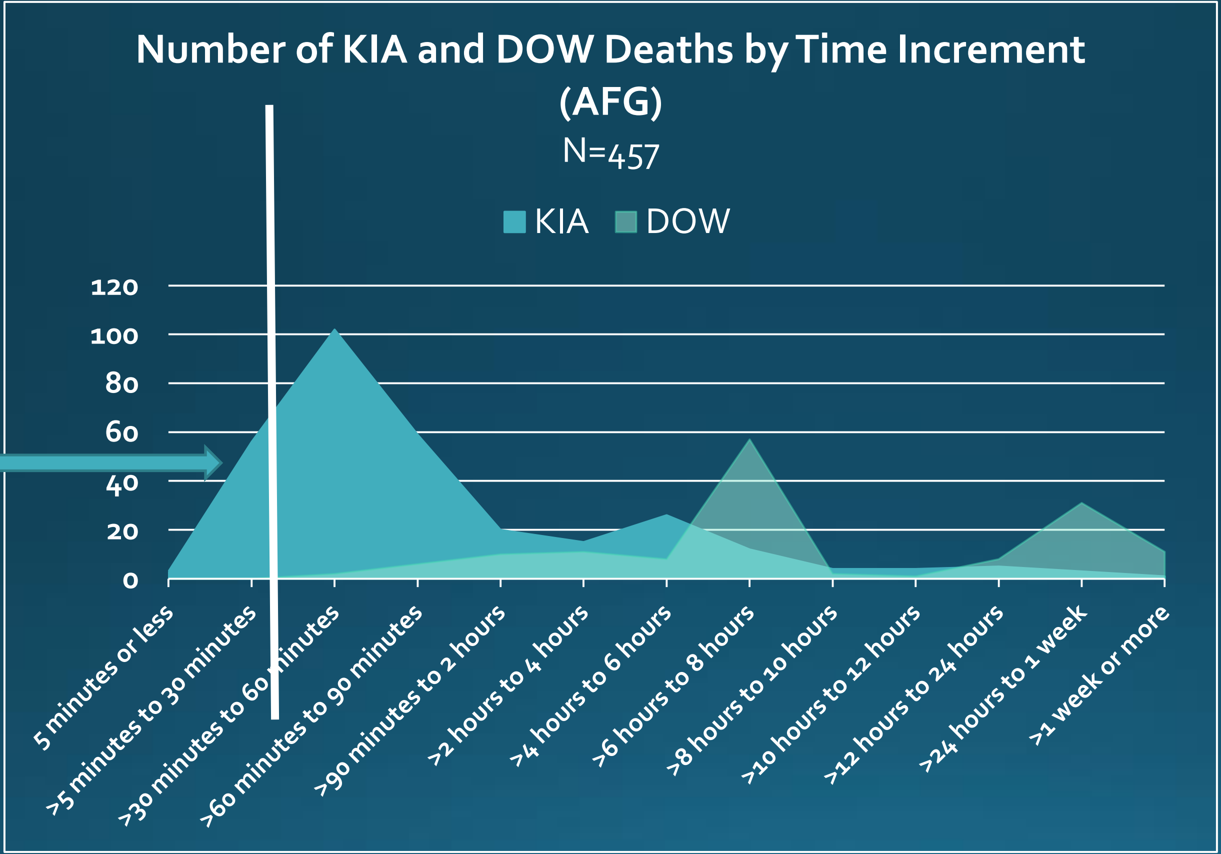
Multicenter observational prehospital resuscitation on helicopter study

John B. Holcomb, MD, Michael D. Swartz, PhD, Stacia M. DeSantis, PhD, Thomas J. Greene, MPH, Erin E. Fox, PhD, Deborah M. Stein, MD, Eileen M. Bulger, MD, Jeffrey D. Kerby, MD, PhD, Michael Goodman, MD, Martin A. Schreiber, MD, Martin D. Zielinski, MD, Terence O'Keeffe, MBChB, MSPH, Kenji Inaba, MD, Jeffrey S. Tomasek, MD, Jeanette M. Podbielski, Savitri N. Appana, MS, Misung Yi, MS, Charles E. Wade, PhD, *and* the PROHS Study Group, *Houston, Texas*

Twenty-five thousand one hundred eighteen trauma patients were admitted, 2,341 (9%) were transported by helicopter, of which 1,058 (45%) met the highest-risk criteria. Five hundred eighty-five of 1,058 patients were flown on helicopters carrying blood products. Unadjusted mortality was significantly higher in the systems with blood products available, at 3 hours (8.4% vs 3.6%), 24 hours (12.6% vs 8.9%), and 30 days (19.3% vs 13.3%). Twenty-four percent of eligible patients received a PHT. A median of 1 unit of RBCs and plasma were transfused Pre-hospital. Of patients receiving PHT, 24% received only plasma, 7% received only RBCs, and 69% received both. In the propensity score matching analysis (n = 109), PHT was not significantly associated with mortality at any time point, although only 10% of the high-risk sample were able to be matched. Because of the unexpected imbalance in systolic blood pressure, Glasgow Coma Scale, and Injury Severity Score between systems with and without blood products on helicopters, matching was limited, and the results of this study are inconclusive.

J Trauma Acute Care Surg. 2017;83: S83–S91

Time to Death: KIA/DOW
Golden Hour is too late to start DCR



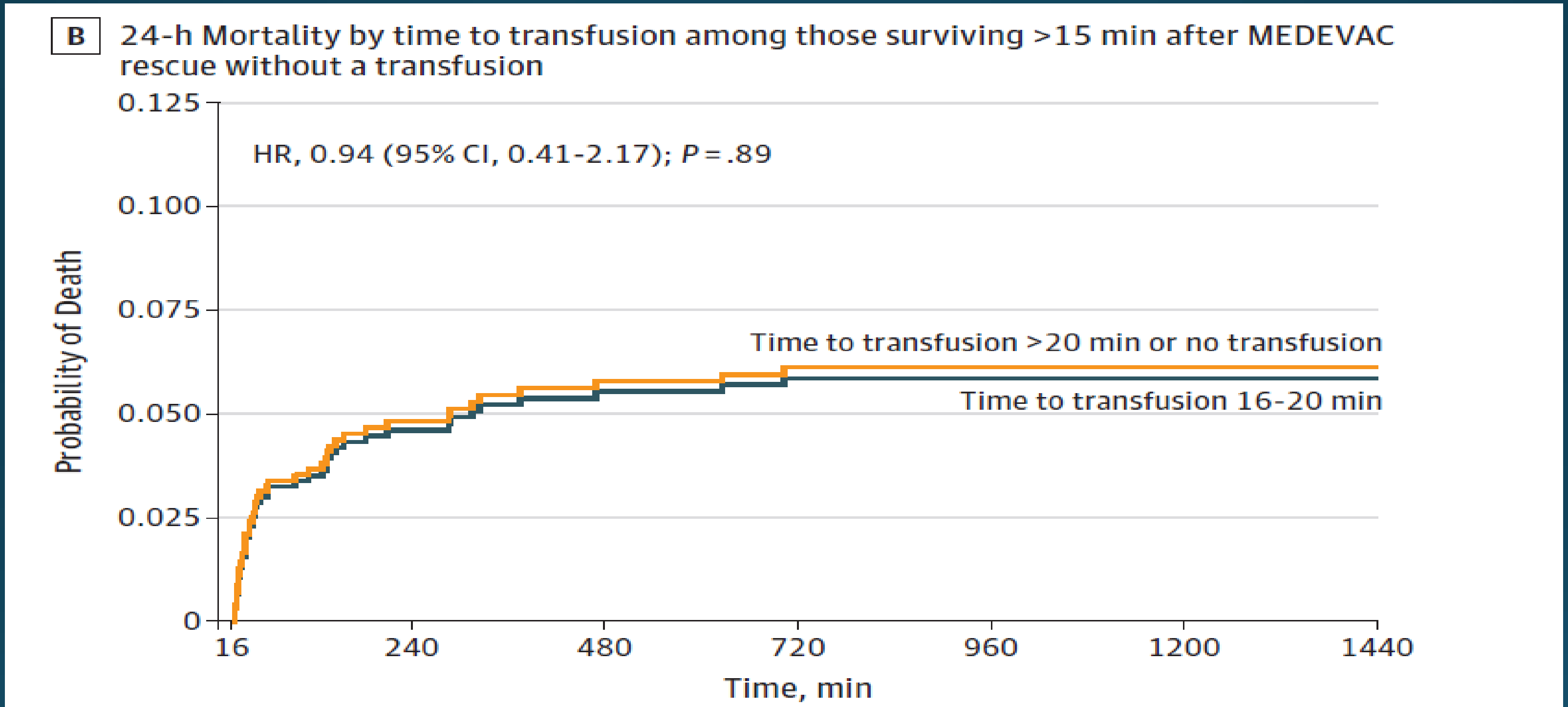
Must Start Resuscitation in the Prehospital Period (RDCR)

Slide Borrowed and Modified from Dr. Andre Cap

Zero Preventable Deaths

- **Spinella and Cap – Curr Opin Hematol 2017; 24:529-535**
- 2010 - 5.1 million trauma-related deaths worldwide
  - Nearly 10% of all deaths
- United States – Trauma
  - Third leading cause of death - All ages
  - Leading cause of death - 1–46 years of age

Shackelford et al - JAMA 2017; 318:1581-1591



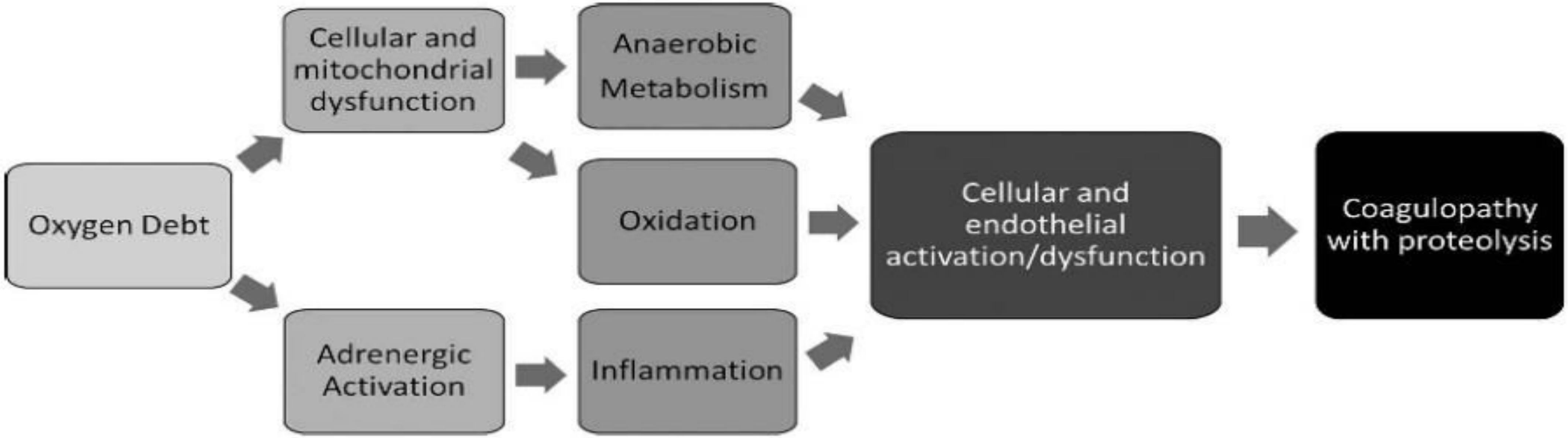


Figure 2. Schematic of key linkages between oxygen debt, cellular dysfunction, and coagulopathy during hemorrhagic blood failure.

J Trauma Acute Care Surg 2017; 82:S41-S49

Rand Analysis – Blood Supply

- Assessed vulnerability of blood supply chain
- Four domains
  1. Magnitude of expected impact on the particular health care market or geographic area
  2. Local vulnerability – Impact in the immediate vicinity of the emergent situation (e.g., New York Blood Center after 9/11/2001 attacks)
  3. Nationwide supply chain risk (e.g., all Blood Centers after 9/11/2001 attacks)
  4. Ability of the nationwide blood supply system to respond quickly to blood and blood supply needs of the event
- Bottom line risk for the blood supply chain system in U.S.
  - Magnitude of the disaster + Ability of system to absorb or mitigate supply or demand shocks

Table 7.8
Summary of Risk Scores

	Scenario 1: Natural Disaster			Scenario 2: Terrorist Attack	Scenario 3: Global Pandemic
Impact	Low	Medium	High	High	Low
Donors	Low	Low	Medium	Low	High
Blood center reserve stocks	Low	Low	Medium	Medium	High
Vendors to blood centers	Low	High	High	High	High
Blood center personnel and equipment	Low	Low	Medium	Medium	High
Critical Infrastructure	Low	Low	Medium	Medium	Medium
Transportation	Low	Medium	High	Medium	Medium
Demand	Low	Low	Medium	Medium	Low

Published by the RAND Corporation, Santa Monica, Calif.

Rand Analysis – Blood Supply

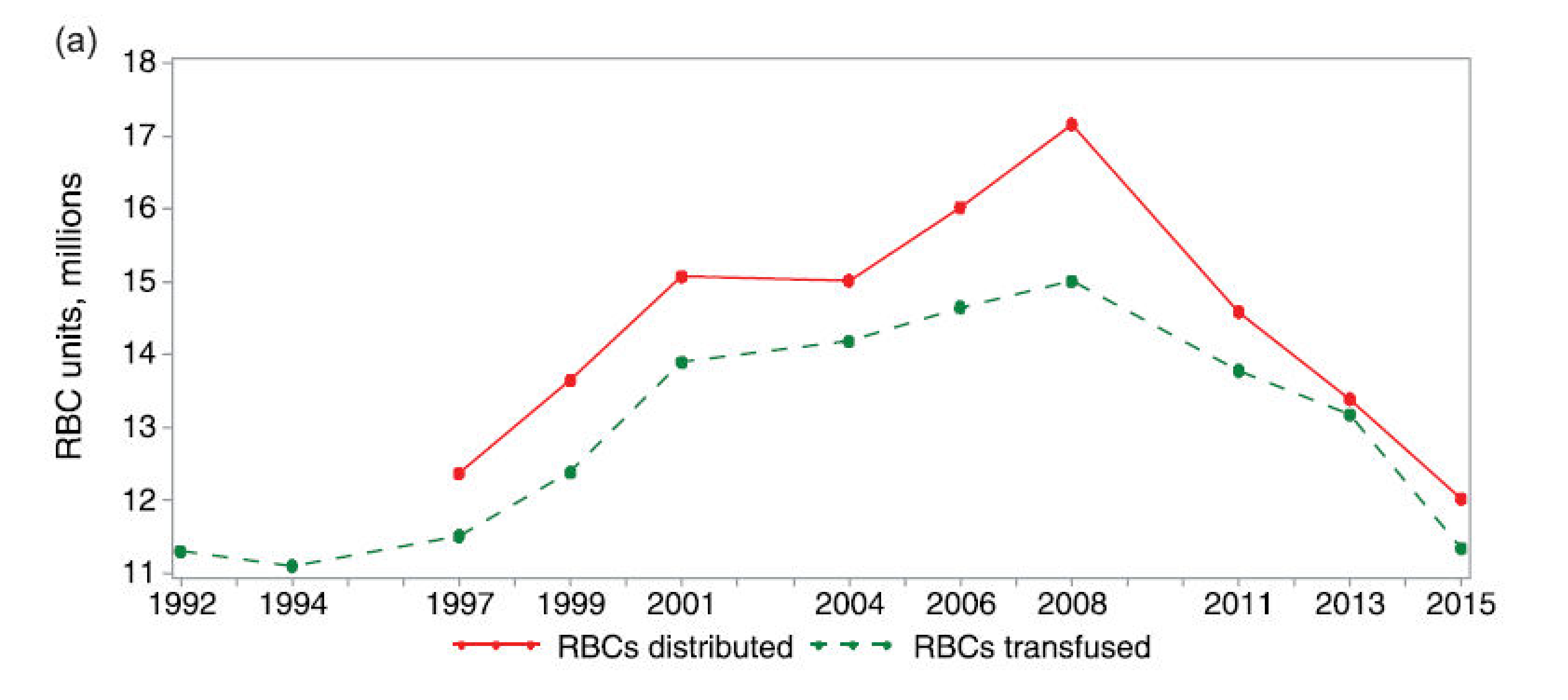
- Conclusions
- To Date - U.S. blood system – Robust enough - Effectively respond to disaster events
- Several areas – Vulnerability – Blood supply chain – Identified
- Particularly noteworthy:
  - Shortage of essential personnel
  - Lack of redundancy in supply vendors.
- Blood Centers - Consider warehousing essential supplies as opposed to just-in-time inventory
- Blood Centers - Advocate for national stockpiles of critical supplies
  - Funded - Government contracts similar to medical countermeasure contracts
- Mitigation - Personnel shortages - More challenging
  - Lower numbers of individuals – Choosing medical science careers

Rand Analysis – Blood Supply

- Terrorist attacks and natural disasters - Problems of surges in demand coupled with potential local shortages
- Such scenarios – Typically local events
  - Surges in demand caused by trauma-related injuries
  - Historically - Absorbed easily by the national system - Despite local shortages
- Key - Such scenarios - Critical infrastructure and transportation issues
- Directly affect - System's ability to move blood both locally and nationally

Rand Report & AABB

- The RAND - Highlights several significant challenges currently facing the blood system:
  - The shrinking donor pool
  - Reduced demand for blood
  - Consolidation throughout the health care system
  - Reduced profits for blood centers and suppliers
  - Workforce shortages
  - Lack of integrated health information technology
  - Barriers to innovation
  - Declining investment in research and development
  - Vulnerabilities to emerging threats and public health emergencies
- In spite of these threats, the report concludes that "the U.S. blood system under the *status quo* operates effectively and in many cases efficiently."



TRANSFUSION 2017;57;1588–1598

Balanced Resuscitation!

Early Platelet Use Important!

An Evaluation of the Impact of Apheresis Platelets Used in the Setting of Massively Transfused Trauma Patients

Jeremy G. Perkins, MD, Cap P. Andrew, MD, PhD, Philip C. Spinella, MD, Lorne H. Blackbourne, MD, Kurt W. Grathwohl, MD, Thomas B. Repine, MD, Lloyd Ketchum, MD, Paige Waterman, MD, Ruth E. Lee, Alec C. Beekley, MD, James A. Sebesta, MD, Andrew F. Shorr, MD, Charles E. Wade, PhD, and John B. Holcomb, MD

Introduction: Trauma is a major cause of morbidity and mortality worldwide. Of patients arriving to trauma centers, patients requiring massive transfusion (MT, ≥10 units in 24 hours) are a small patient subset but are at the highest risk of mortality. Transfusion of appropriate ratios of blood products to such patients has recently been an area of interest to both the civilian and military medical community. Plasma is increasingly recognized as a critical component, though less is known about appropriate ratios of platelets. Combat casualties managed at the busiest combat hospital in Iraq provided an opportunity to examine this question.

Methods: In-patient records for 8,618 trauma casualties treated at the military hospital in Baghdad more than a 3-year interval between January 2004 and December 2006 were retrospectively reviewed and patients requiring MT (n = 694) were identified. Patients who required MT in the first 24 hours and did not receive fresh whole blood were divided into study groups defined by source of platelets: (1) patient receiving a low ratio of platelets (<1:16 apheresis platelets per stored red cell unit, aPLT:RBC) (n = 214), (2) patients receiving a medium ratio of platelets (1:16 to <1:8 aPLT:RBC) (n = 154), and (3) patients receiving a high ratio of platelets (≥1:8 aPLT:RBC) (n = 96). The primary endpoint was survival at 24 hours and at 30 days.

Results: At 24 hours, patients receiving a high ratio of platelets had higher survival (95%) as compared with patients receiving a medium ratio (87%) and patients receiving the lowest ratio of platelets (64%) (log-rank $p = 0.04$ and $p < 0.001$, respectively). The survival benefit for the high and medium ratio groups remained at 30 days as compared with those receiving the lowest ratio of platelets (75% and 60% vs. 43%, $p < 0.001$ for both comparisons). On multivariate regression, plasma:RBC ratios and aPLT:RBC were both independently associated with improved survival at 24 hours and at 30 days.

Conclusion: Transfusion of a ratio of ≥1:8 aPLT:RBC is associated with improved survival at 24 hours and at 30 days in combat casualties requiring a MT within 24 hours of injury. Although prospective study is needed to confirm this finding, MT protocols outside of investigational research should consider incorporation of appropriate ratios of both plasma and platelets.

Key Words: Apheresis platelets, Penetrating injury, Component therapy, Massive transfusion, Combat trauma.

J Trauma. 2009;66:S77–S85.

J Trauma 2009; 66:S77-S85

Ten-year analysis of transfusion in Operation Iraqi Freedom and Operation Enduring Freedom: Increased plasma and platelet use correlates with improved survival

Heather F. Pidcoke, MD, James K. Aden, PhD, Alejandra G. Mora, Matthew A. Borgman, MD, Philip C. Spinella, MD, Michael A. Dubick, PhD, Lorne H. Blackbourne, MD, Andrew P. Cap, MD, PhD

BACKGROUND: The Joint Theater Trauma Registry database, begun early in Operation Iraqi Freedom and Operation Enduring Freedom, created a comprehensive repository of information that facilitated research efforts and produced rapid changes in clinical care. New clinical practice guidelines were adopted throughout the last decade. The damage-control resuscitation clinical practice guideline sought to provide high-quality blood products in support of tissue perfusion and hemostasis. The goal was to reduce death from hemorrhagic shock in patients with severe traumatic bleeding. This 10-year review of the Joint Theater Trauma Registry database reports the military's experience with resuscitation and coagulopathy, evaluates the effect of increased plasma and platelet (PLT)–to–red blood cell ratios, and analyzes other recent changes in practice.

METHODS: Records of US active duty service members at least 18 years of age who were admitted to a military hospital from March 2003 to February 2012 were entered into a database. Those who received at least one blood product (n = 3,632) were included in the analysis. Data were analyzed with respect to interactions within and between categories (demographics, admission characteristics, hospital course, and outcome). Transfusions were analyzed with respect to time, survival, and effect of increasing transfusion ratios.

RESULTS: Coagulopathy was prevalent upon presentation (33% with international normalized ratio $\geq$ 1.5), correlated with increased mortality (fivefold higher), and was associated with the need for massive transfusion. High transfusion ratios of fresh frozen plasma and PLT to red blood cells were correlated with higher survival but not decreased blood requirement. Survival was most correlated with PLT ratio, but high fresh frozen plasma ratio had an additive effect (PLT odds ratio, 0.22).

CONCLUSION: This 10-year evaluation supports earlier studies reporting the benefits of damage-control resuscitation strategies in military casualties requiring massive transfusion. The current analysis suggests that defects in PLT function may contribute to coagulopathy of trauma. (*J Trauma Acute Care Surg*. 2012;73: S445–S452. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Epidemiologic study, level IV.

KEY WORDS: Transfusion ratio; coagulopathy; massive transfusion; OIF; OEF.

J Trauma Acute Care Surg 2012; 73:S445-S452

Andrew P. Cap, MD, PhD, Philip C. Spinella, MD, Matthew A. Borgman, MD, Lorne H. Blackbourne, MD, *and* **Jeremy G. Perkins, MD,** *Fort Sam Houston, Texas*

BACKGROUND: Hemostatic resuscitation using blood components in a 1:1:1 ratio of platelets:fresh frozen plasma:red blood cells (RBCs) is based on analyses of massive transfusion (MT, ≥10 RBC units in 24 hours). These 24-hour analyses are weakened by survival bias and do not describe the timing and location of transfusions. Mortality outcomes associated with early (first 6 hours) resuscitation incorporating platelets, for combat casualties requiring MT, have not been reported.

METHODS: We analyzed records for 8,618 casualties treated at the United States military hospital in Baghdad, Iraq, between January 2004 and December 2006. Patients (n = 414) requiring MT, not receiving fresh whole blood, and surviving at least 1 hour (reducing survival bias) were divided into 6-hour apheresis platelet (aPLT) transfusion ratio groups: LOW (aPLT:RBC, ≤0.1, n = 344) and HIGH (aPLT:RBC, >0.1, n = 70). Baseline characteristics of groups were compared. Factors influencing survival on univariate analysis were included in Cox proportional hazards models of 24-hour and 30-day survival.

RESULTS: Patients received aPLT in the emergency department (4%), operating room (45%), intensive care unit (51%). The HIGH group presented with higher ($p < 0.05$) admission International Normalized Ratio (1.6 vs. 1.4), base deficit (8 vs. 7), and temperature (36.7 vs. 36.4). Overall mortality was 27%. At 24 hours, the HIGH group showed lower mortality (10.0% vs. 22.1%, $p = 0.02$). Absolute differences in 30-day mortality were not significant (HIGH, 18.6%; LOW, 28.8%, $p = 0.08$). On adjusted analysis, the HIGH group was independently associated with increased survival: LOW group mortality hazard ratios were 4.1 at 24 hours and 2.3 at 30 days compared with HIGH group ($p = 0.03$ for both). Increasing 6-hour FFP:RBC ratio was also independently associated with increased survival.

CONCLUSION: Early (first 6 hours) hemostatic resuscitation incorporating platelets and plasma is associated with improved 24-hour and 30-day survival in combat casualties requiring MT. (*J Trauma Acute Care Surg*. 2012;73: S89–S94. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Therapeutic study, level III.

KEY WORDS: Apheresis platelets; resuscitation; massive transfusion; combat trauma.

J Trauma Acute Care Surg 2012; 73:S89-S94

TABLE 2. Estimated number of platelets, plasma, and cryoprecipitate units distributed, transfused, and outdated in 2015 (expressed in thousands)

Variable	Blood centers	Hospitals	Combined totals	95% CI	2013 Totals*	% Change 2015-2013
Distributed						
Apheresis platelets	2034	200	2234	2040-2429	2318	−3.6
Whole-blood–derived PLTs†	189	13	202	146-257	130	55.0
Total platelets	2223	213	2436	2230-2642	2448	−0.5
Total plasma	3450	264	3714	3306-4121	4338	−14.4
Cryoprecipitate‡	1694	163	1857	1605-2109	978	89.9
Blood center outdates§	217	25	242	211-273	239	1.2
Transfused						
Apheresis platelets		1807		1670-1943	2137	−15.4
Whole-blood–derived PLTs†		171		84-258	128	33.7
Total platelets (includes directed units)		1983		1816-2151	2281	−13.1
Total plasma		2727		2594-2859	3624	−24.8
Cryoprecipitate‡		1167		1021-1314	1095	6.6
Hospital outdates‖		426		392-461	395	7.9

TRANSFUSION 2017;57;1588–1598

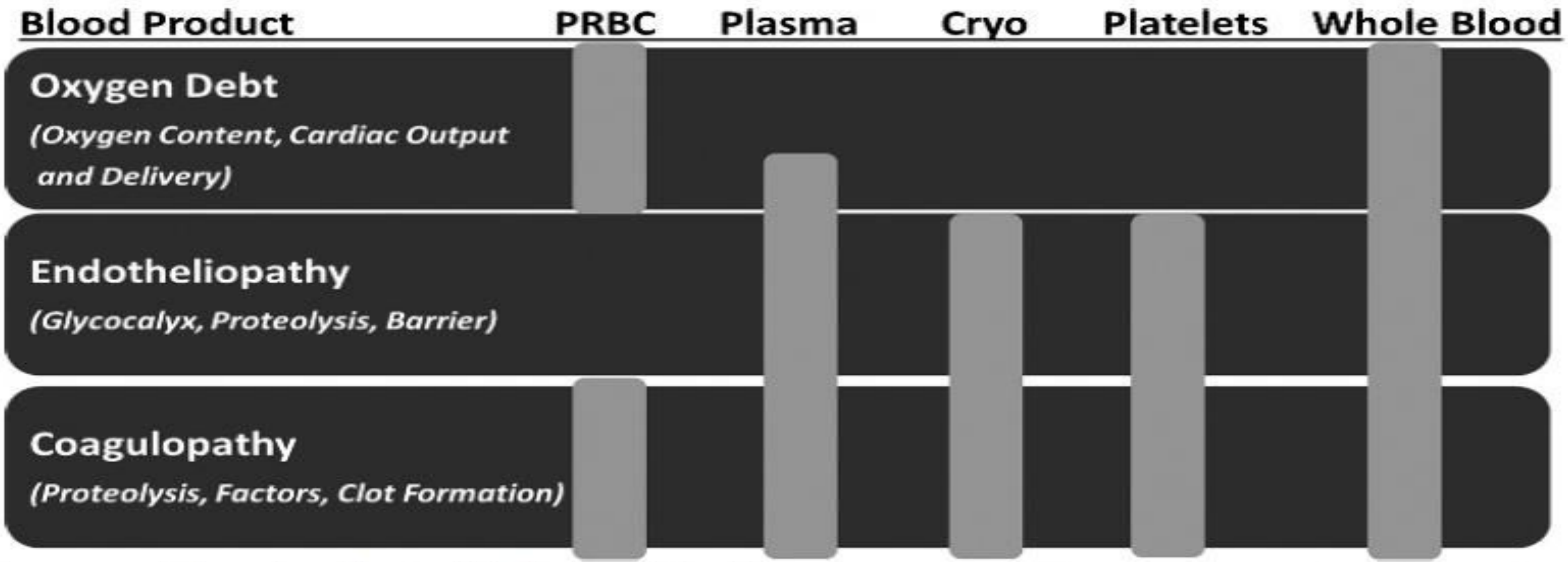


Figure 3. Schematic summarizing the effects of individual blood products on the three components of hemorrhagic blood failure. PRBC, packed red blood cells; Cryo, cryoprecipitate.

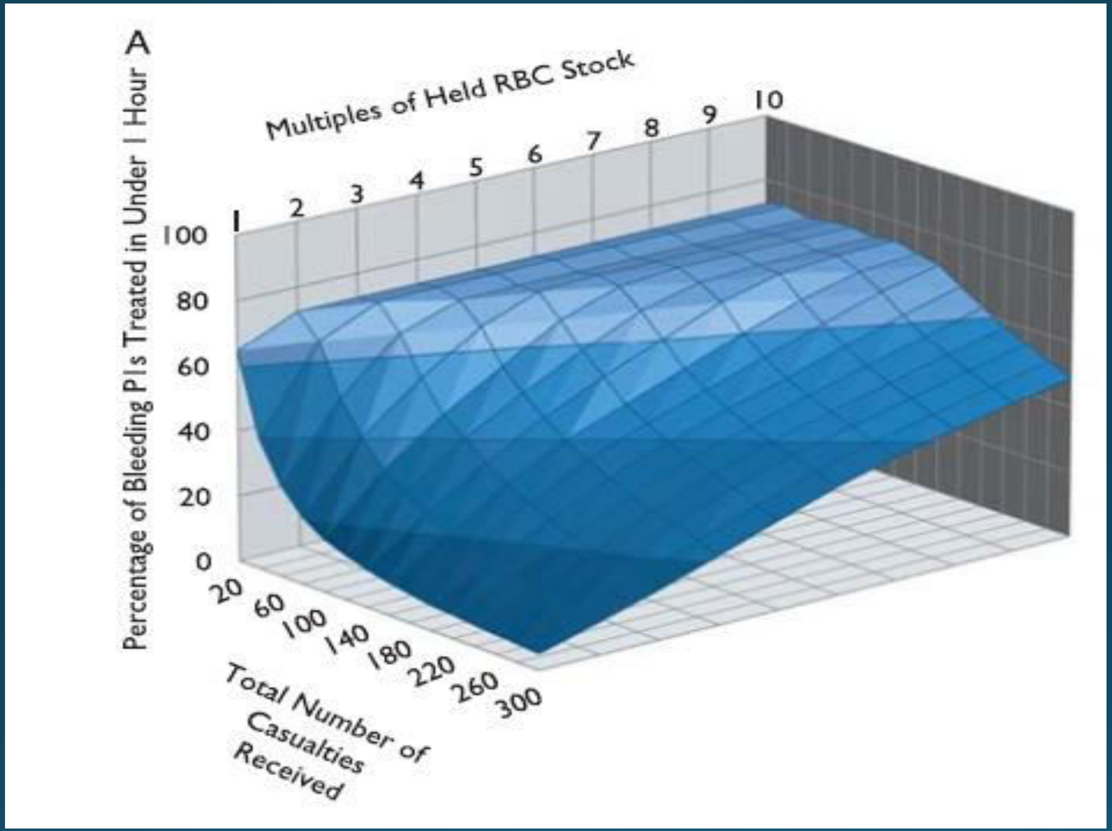
J Trauma Acute Care Surg 2017; 82:S41-S49

RBC								
	A Neg	A Pos	AB Neg	AB Pos	B Neg	B Pos	O Neg	O Pos
Daily Usage	5.9	23.3	0.5	1.7	1.4	5.8	8.9	31.3
Target Capacity (Days)	12	12	12	12	12	12	12	12
Target Inventory								
Optimum	71	280	6	20	17	69	107	375
Minimum	53	210	5	15	12	52	81	282
Critical	35	140	3	10	8	35	54	188

FFP					
	A	AB	B	O	AB Peds
Daily Usage	15.2	2.0	3.5	8.1	NA
Target Capacity (Days)	60	60	60	60	NA
Target Inventory					
Optimum	913	117	207	486	10
Minimum	639	82	145	340	NA
Critical	457	59	104	243	
Keep 10 units at the hospital and hold at least10 Peds units in CO.					

Platelets	
Target Capacity (Days)	2
Rh Negative Units	25%

Platelets don’t have a standing number, just 2 days of inventory based on the day of week and past four weeks usage



J Trauma Acute Care Surg 2016;81: 50–57

Managing the Surge in Blood Demand

- Model reinforced findings - Previous studies - Capacity of trauma centers – Cope - More limited than we would like to think!
- Standard stock – 210 RBCs units – Inadequate - Casualty loads as low as 20
- Correlated - RBC consumption of 160 units - Seven bleeding casualties – 2005 London bombings
  - Multiple RBC restocks occurred
- Achieving acceptable levels of care – Model – Require - Significant increase - Blood component availability
  - Most notably - Emergency group O RBCs.
  - When group O RBC supplies begin to exhaust – Ability - Effectively manage casualties rapidly deteriorates
- Number of group O RBCs and the rate of consumption – Likely - Best indication – Transfusing facility - Reaching surge capacity.

The state of the science of whole blood: lessons learned at Mayo Clinic

James R. Stubbs,[1] Martin D. Zielinski,[2] and Donald Jenkins[2]

TRANSFUSION 2016;56;S173–S181

Whole Blood Program Started in 2015

Cold platelets for trauma-associated bleeding: regulatory approval, accreditation approval, and practice implementation—just the "tip of the iceberg"

James R. Stubbs,[1] Sheryl A. Tran,[2] Richard L. Emery,[1] Scott A. Hammel,[1] De Anna L. Haugen,[3] Martin D. Zielinski,[4] Scott P. Zietlow,[4] and Donald Jenkins[4]

Transfusion 2017; 57:2836-2844

Cold Platelet Program Started in 2015

THE FEASIBILITY OF A WARM FRESH WHOLE BLOOD DONATION PROGRAM IN A CIVILIAN HEALTH SYSTEM

Joy D. Hughes MD, Matthew C Hernandez MD, Mariela Rivera MD, FACS, Mark Sawyer, MD, FACS, Justin D. Kreuter, James R. Stubbs, MD, Martin D. Zielinski, MD, FACS*

In Preparation