

**Emergency transfusion:**  
**We issued the uncrossmatched  
RBCs, now what do we do?**

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## Goals for today's presentation:

- Epidemiology of trauma
- Military: “Damage control resuscitation”
- 1:1:1 resuscitation and ‘survivorship bias’
- The acute coagulopathy of trauma
- CRASH-2
- TEG / ROTEM
- The Canadian Consensus Conference on Massive Transfusion

Trauma is a brutal, unexpected, tragedy that spares no age group.

Excluding adverse events in medical care...

Trauma is...

- The leading cause of death for those aged 1 – 44.
- 4<sup>th</sup> leading cause of death for Canadians of all ages.
- The leading cause of potential years of life lost.

Facts on Injury:

<http://www.phac-aspc.gc.ca/injury-bles/facts-eng.php>.

## A SHOT incident....Policy for RBC release

*“A patient showed signs of haemorrhagic shock and haemoglobin was 4.0 g/dl. Urgent blood transfusion and surgical review was indicated. Despite the clinical condition of the patient the hospital transfusion policy allowed them to issue only one unit at a time. Two units were issued once it was made clear that the patient was going to theatre.”*

## A SHOT incident... Coagulation factors

*“A patient bled in excess of half her circulating volume from her chest via a drain in a little over 15 minutes and developed all the classical symptoms of hypovolaemic shock. Within minutes she had been transfused 4 units of packed red cells and transferred to theatre.*

*She received a further 12 units of packed red cells and 6 litres of other fluids. There are no clotting factors in any of this. Initial requests to the hospital transfusion laboratory for blood components led to a referral to Dr [Staff Name] who initially refused on the basis that the previous coagulation tests had been normal.”*

## SHOT incident.... Porter issue

*“A patient became acutely unwell on the ward and at 1015 we became aware that Hb was 3.8 g/dl. The medical team requested that 10 units be crossmatched at 10:20 hrs and the porters were immediately asked to urgently collect 4 units and bring to the ward.*

*Despite 3 follow up calls the blood wasn't signed out of the lab until 10:47 and didn't reach the ward until 11:05hrs, some 50 minutes after the request call.*

*Only 1 unit was brought not the 4 needed for rapid transfusion”.*

# The wars in Iraq and Afghanistan

## Damage Control Resuscitation

“Newer transfusion protocols, based on research from the War on Terror,...

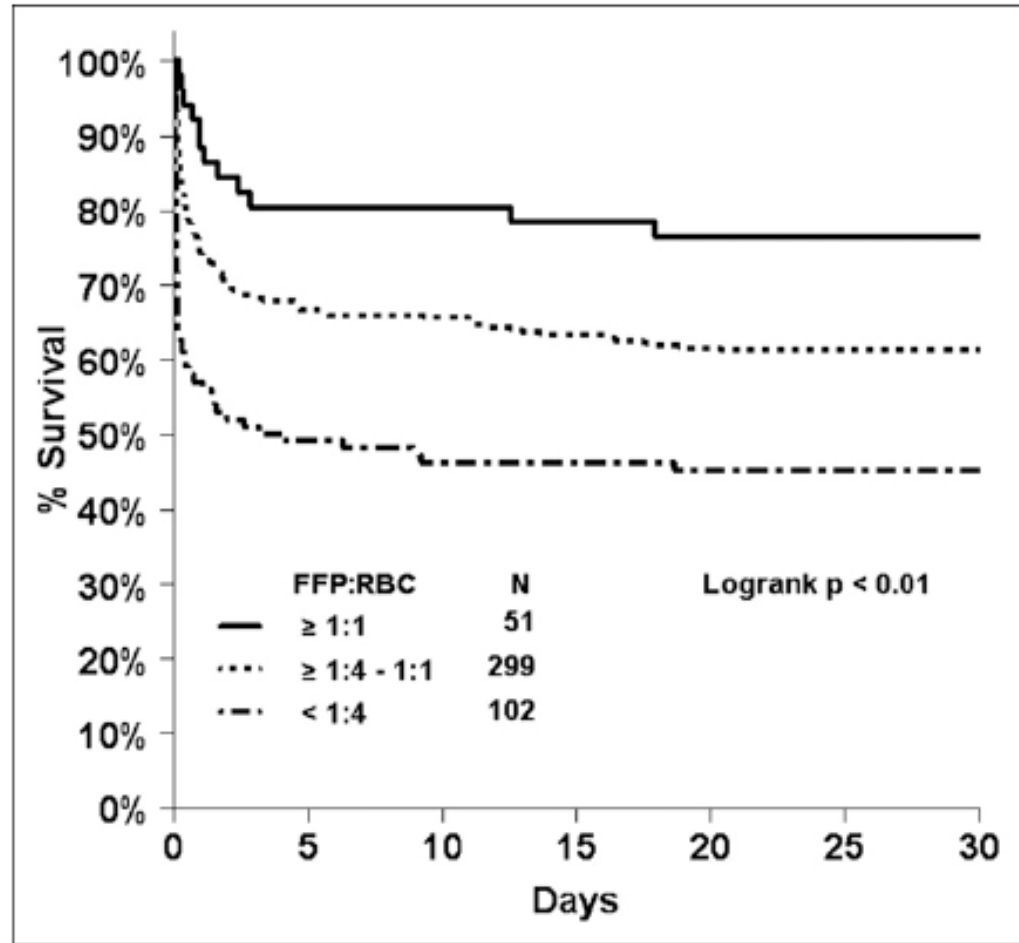
The concept of damage control resuscitation...encompasses:

- \* rapid surgical correction of large vessel bleeding;
- \* prevention and treatment of acidosis and hypothermia;
- \* transfusion of plasma, RBCs, and platelets in a 1:1:1 ratio;
- \* early use of fibrinogen;
- \* potential use of rVIIa; and
- \* decreased emphasis on excessive crystalloid and RBC use.

# 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

Karen A. Zink, M.D., Chitra N. Sambasivan, M.D., John B. Holcomb, M.D., Gary Chisholm, Ph.D., Martin A. Schreiber, M.D.\*

Retrospective review of 452 patients receiving >10 units RBCs in 24 hours



# Retrospective studies of FFP to RBC ratios

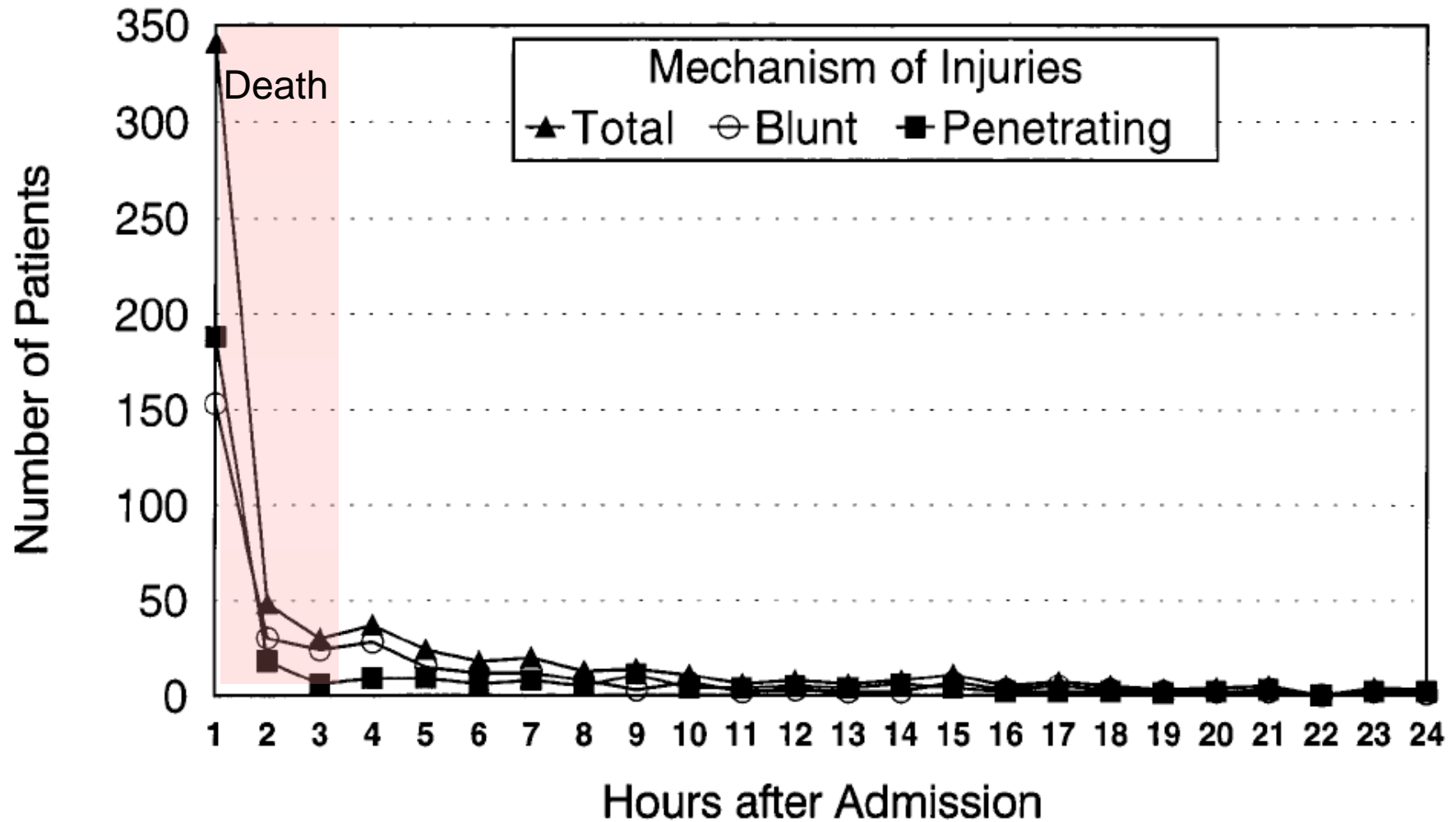
Author	'n'	Benefit (HR)	
Duchesne, 2008	135	18.9 (6.3-56.4)	
Gunter, 2008	259	1.8 (1.0-3.1)	
Holcomb, 2008	466	60% vs 40%	
Kashuk, 2008	133	U-shaped	
Maegele, 2008	713	76% vs 54%	
Sperry, 2008	415	2.1 (1.3-3.3)	
Teixeira, 2009	383	3.5 (2.5-4.8)	
Zink, 2009	452	74% vs 45%	
Snyder, 2009	134	1.2 (0.7-2.1)	95% confidence interval shows no significant effect
Magnotti, 2011	103	1.8 (0.9-3.6)	

# Survivorship Bias

- In situations where most patients die early in treatment.....
- If RBCs are consistently transfused before FFP.... then, patients who die early will not survive long enough to receive FFP (RBCs > FFP), whereas those who live long enough to receive FFP will have RBC similar to FFP.
- “FFP does not lead to survival; rather survival allows time to receive FFP.”

# Lethal Injuries and Time to Death in a Level I Trauma Center

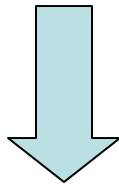
José A Acosta, MD, FACS, Jack C Yang, MD, Robert J Winchell, MD, FACS, Richard K Simons, MB, FACS, Dale A Fortlage, BA, Peggy Hollingsworth-Fridlund, RN, and David B Hoyt, MD, FACS



# The Relationship of Blood Product Ratio to Mortality: Survival Benefit or Survival Bias?

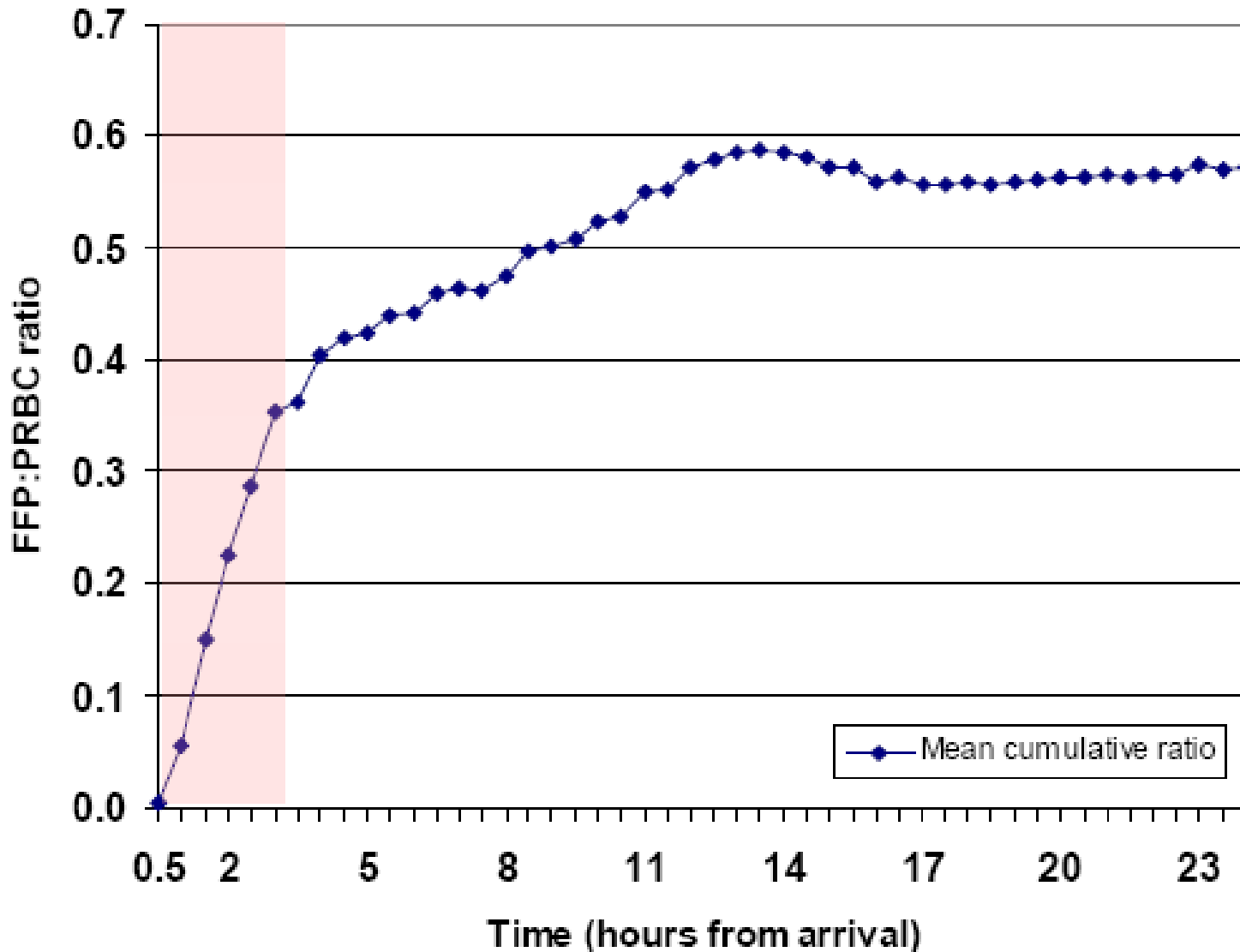
*Christopher W. Snyder, MD, Jordan A. Weinberg, MD, Gerald McGwin, Jr., MS, PhD, Sherry M. Melton, MD, Richard L. George, MD, Donald A. Reiff, MD, James M. Cross, MD, Jennifer Hubbard-Brown, BS, Loring W. Rue, III, MD, and Jeffrey D. Kerby, MD, PhD* *J Trauma.* 2009;66:358–364.

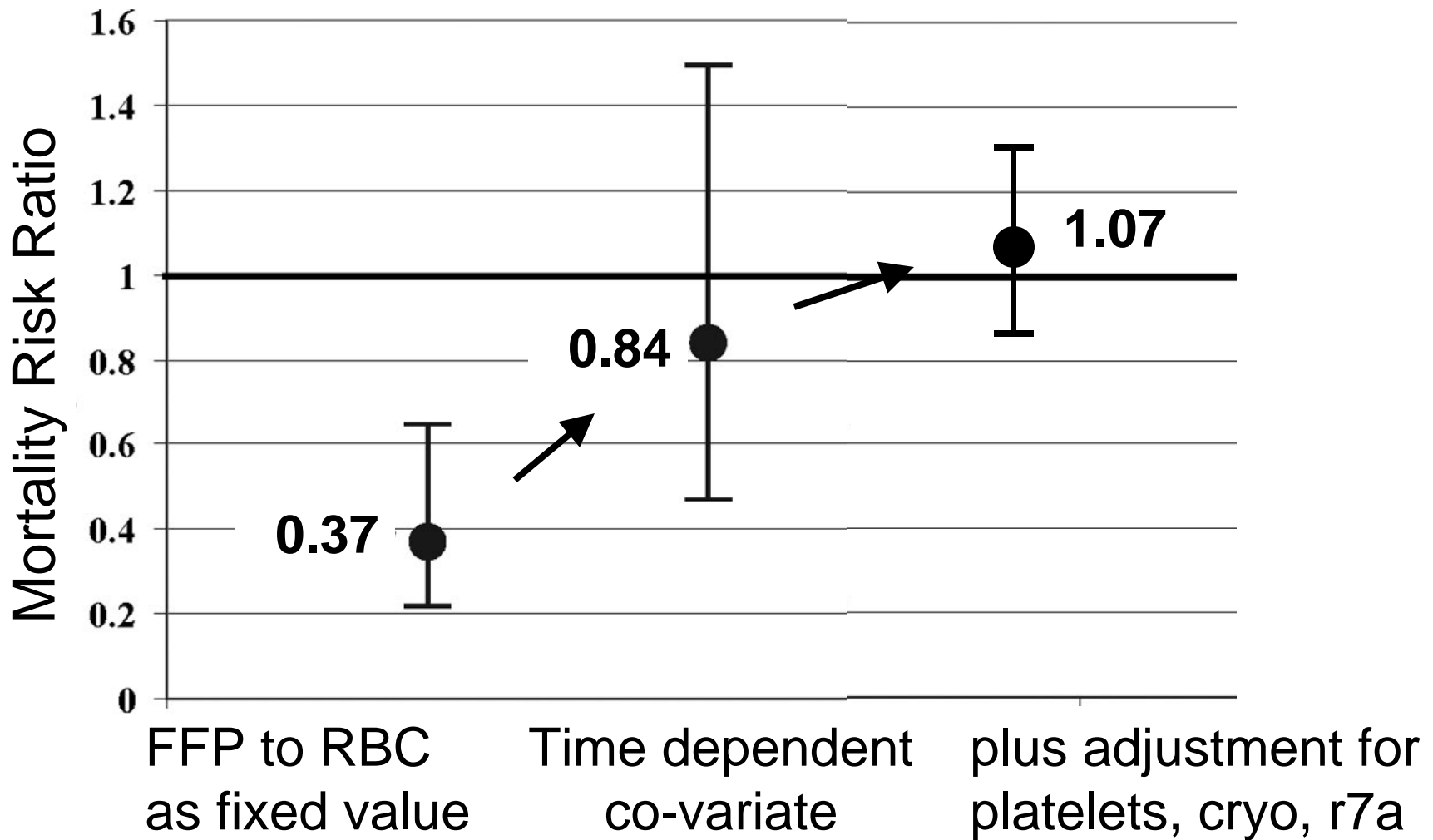
- \* Trauma patients, n= 134, with >10 RBCs in 24 hours
- \* January 2005 to January 2007.
- \* Data from trauma bay nursing flow sheets, OR anesthesia record, and ICU records. .
- \* Chart review records TIME of admission, transfusions, and death.



- \* FFP and RBC ratios determined for each patient.

# FFP-to-RBC ratio is a time dependent variable





“Therefore, it could be concluded that the non-survivors in our study population did not die because they got a lower FFP-to-RBC ratio; rather, they got a lower ratio because they died.”

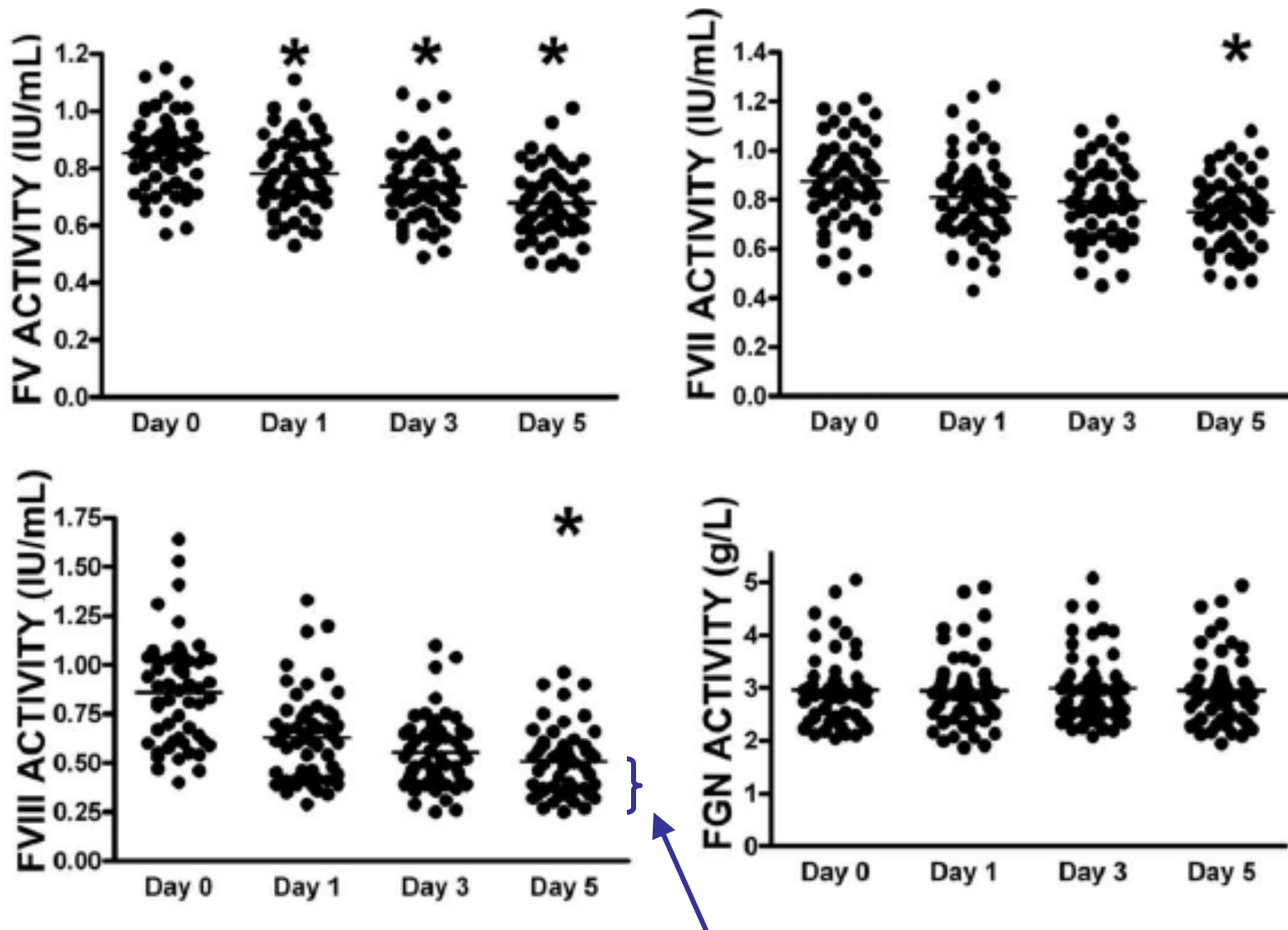
# Retrospective studies of FFP to RBC ratios

Author	'n'	Benefit (HR)	Correction for bias
Duchesne, 2008	135	18.9 (6.3-56.4)	No
Gunter, 2008	259	1.8 (1.0-3.1)	No
Holcomb, 2008	466	60% vs 40%	Excluded 1 death in 30'
Kashuk, 2008	133	U-shaped	No
Maegele, 2008	713	76% vs 54%	Excluded pre-ICU deaths
Sperry, 2008	415	2.1 (1.3-3.3)	No
Teixeira, 2009	383	3.5 (2.5-4.8)	No
Zink, 2009	452	74% vs 45%	No
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# Practical effects of 1:1 on the transfusion service

- Stocking of group O RBCs and AB plasma in ER
- Increase use of AB plasma
- Increase in cases with “no ABO sample”
- Converting all plasma from FFP to 5 day “thawed plasma
- A lot more FFP is given... ? adverse effects

# Decline in factor levels in thawed plasma

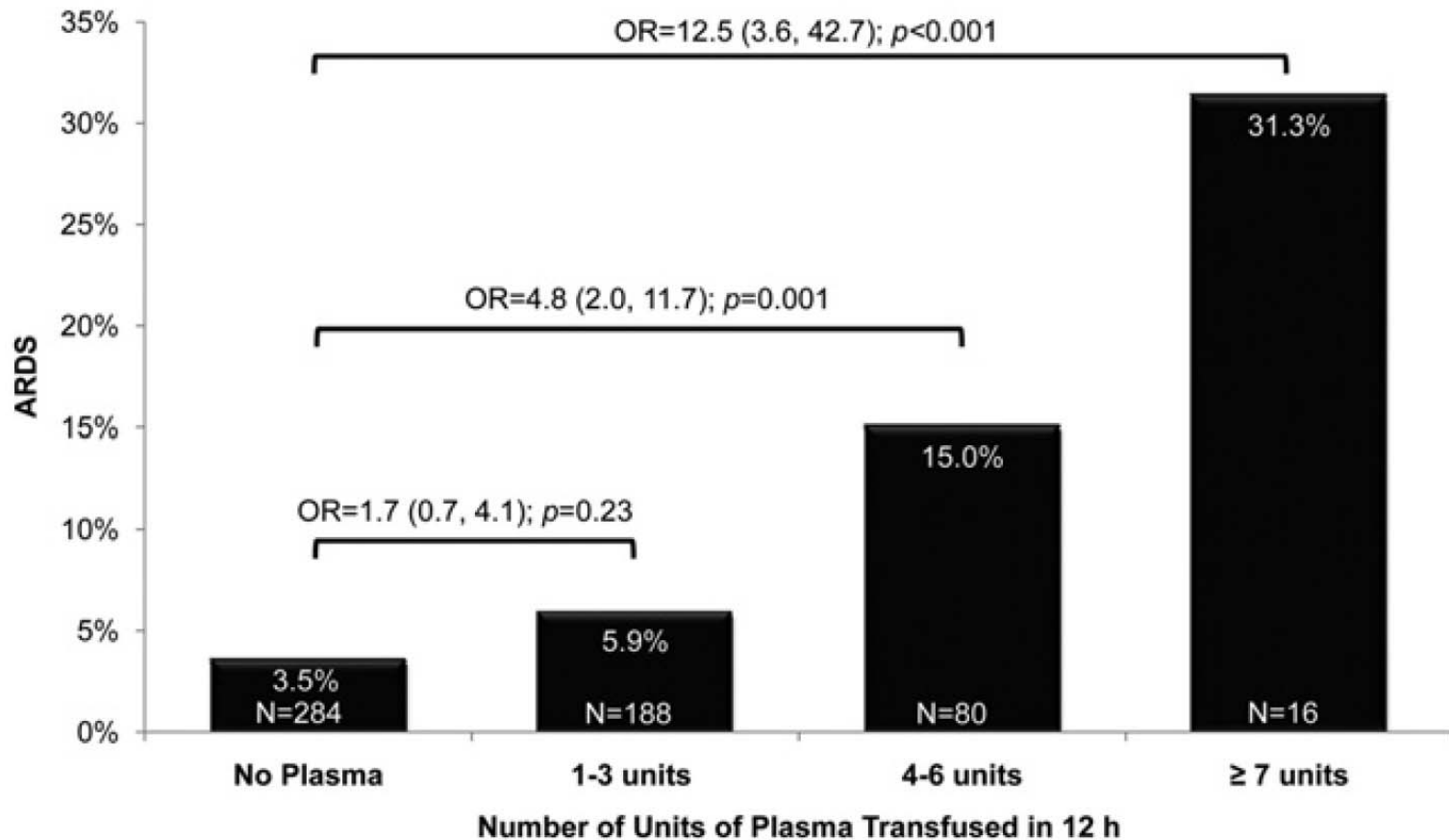


50% of units have factor VIII levels < 50%

## Effects on those without massive transfusion

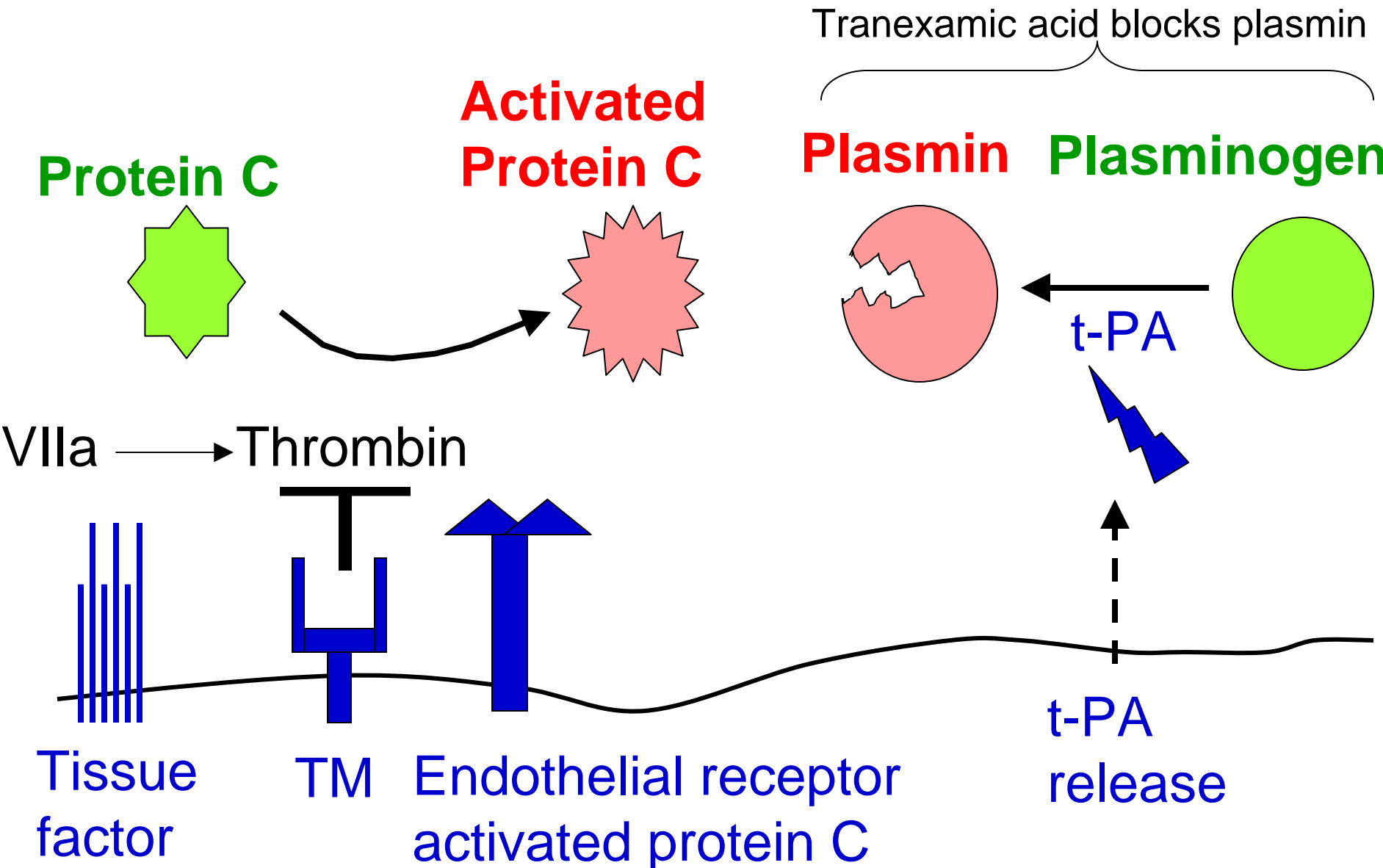
- Retrospective review of 1933 trauma patients.
- n=1716: receive < 10 RBCs/24 hours
- Compared two matched groups:
  - n=284 who receive FFP
  - n=284 with no FFP.
- Survival:
  - With FFP: 17.3 %
  - Without FFP: 14.1 %
- FFP was associated with higher risk of complications:
  - ARDS (12-fold);
  - MOF (6-fold);
  - pneumonia/sepsis (4-fold)

# Excess plasma is associated with higher risk of ARDS



**Figure 3.** ARDS rates stratified by the number of units of plasma transfused in 12 hours. OR, odds ratio (95% confidence interval); p-values were derived from McNemar's chi-square test.

# Fibrinolysis is the vascular response to injury and shock



# Implications of the 'new' model

- The initial coagulopathy is not “dilutional”.
- FFP (up front) may actually be detrimental: infusing plasminogen and protein C— both substrates for anticoagulant pathways.
- Fibrinogen sources:
  - FFP and PCC contain Protein C.
  - Cryoprecipitate and Fibrinogen concentrate do not contain Protein C.
- Inhibitors of fibrinolysis should be effective as an “up front” therapy

# CRASH-2

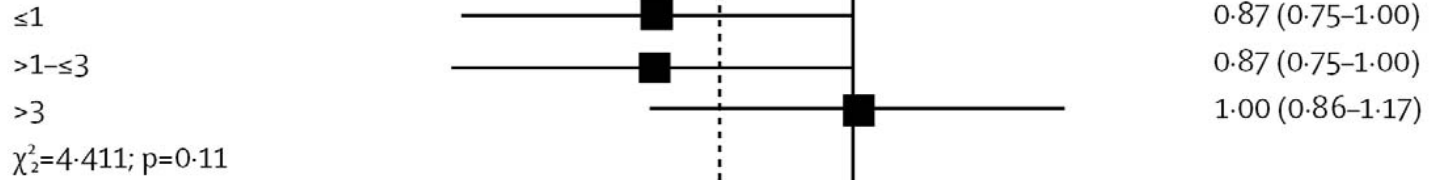
- Multicenter, prospective randomized trial
- 274 hospitals in 40 countries.
- n = 20,211 injured patients randomized to:
  - tranexamic acid: 1 gm bolus & 1 gm in 8 hrs
  - vs, placebo infusion.
- Primary outcome: Death in hospital within 4 weeks
  - Tranexamic: 14.5%
  - Placebo: 16%

} p < 0.0035
- Secondary outcome: bleeding-related death
  - Tranexamic: 4.9%
  - Placebo: 5.7

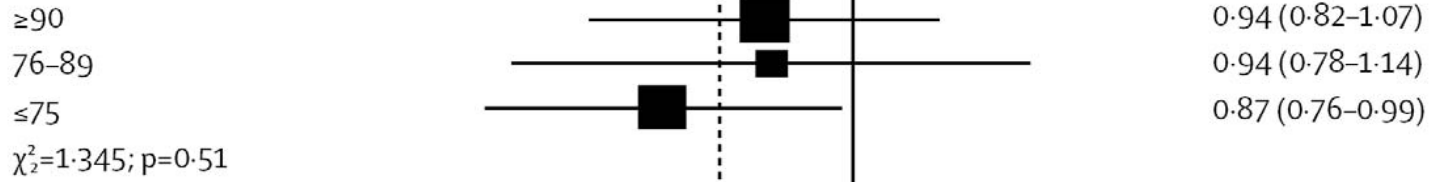
} p < 0.0077

Risk ratio (99% CI)

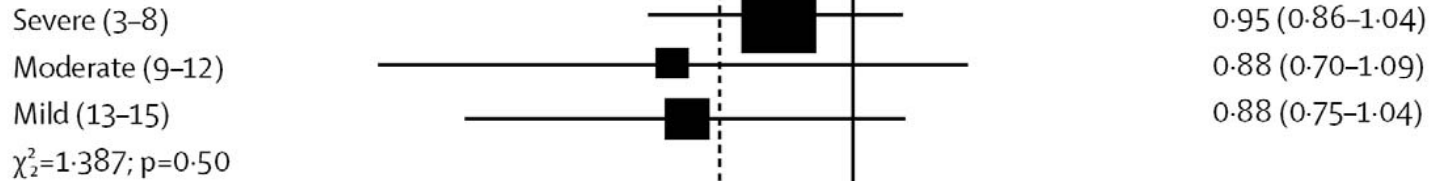
Time from injury (h)



Systolic blood pressure



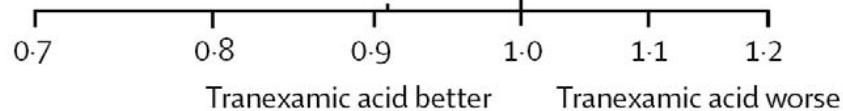
GCS



Injury type



All patients

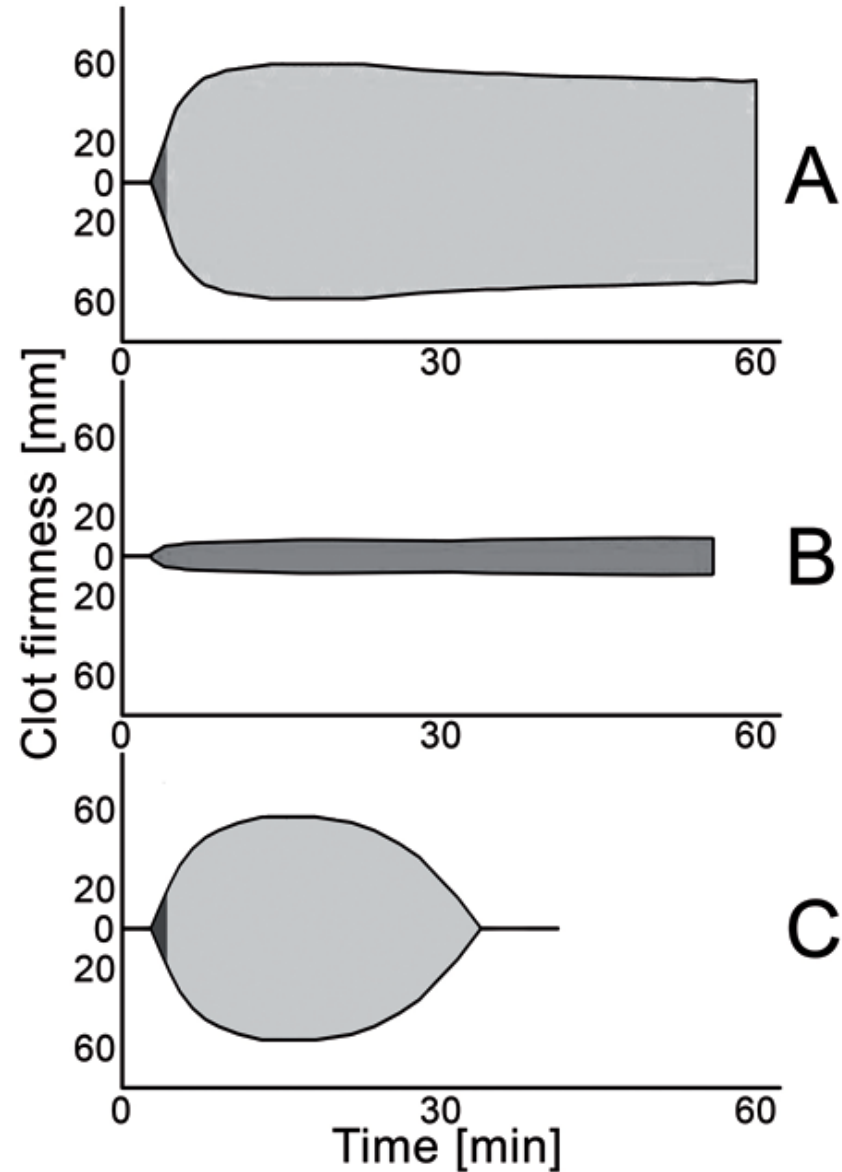
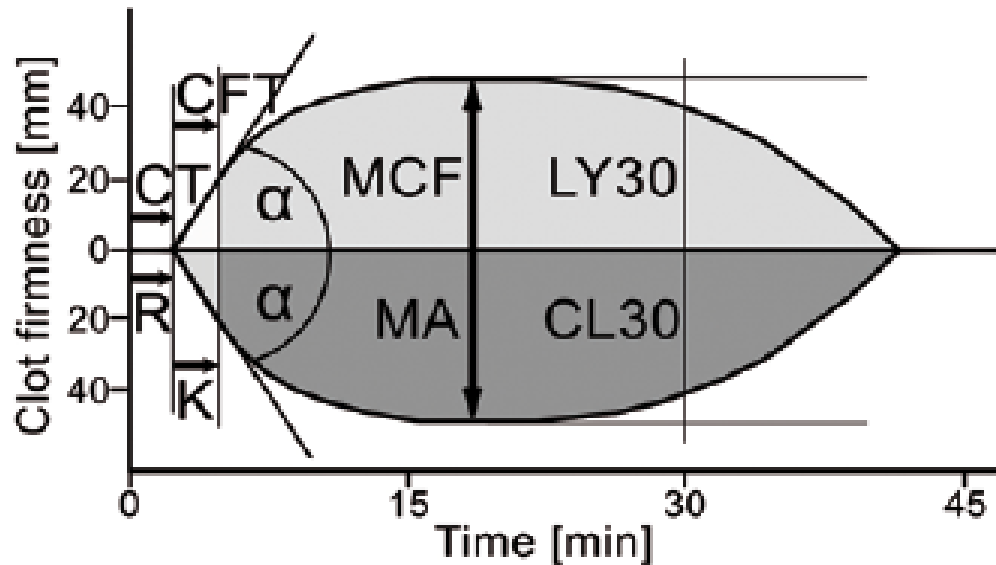
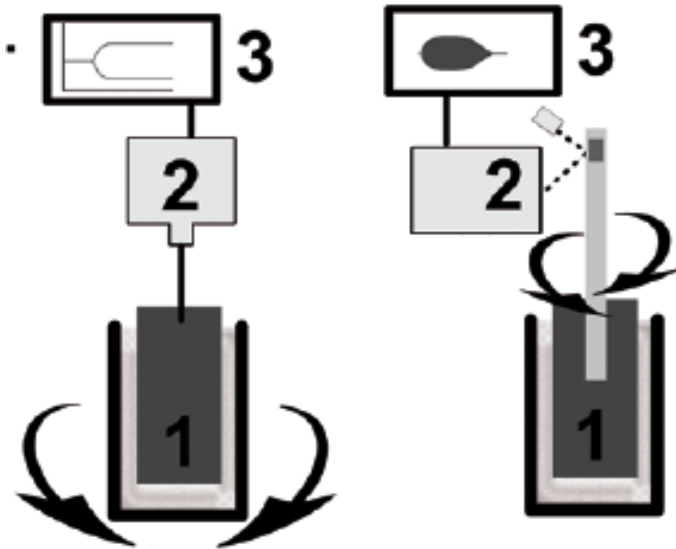


Better if TxA is given within 3 hours of injury

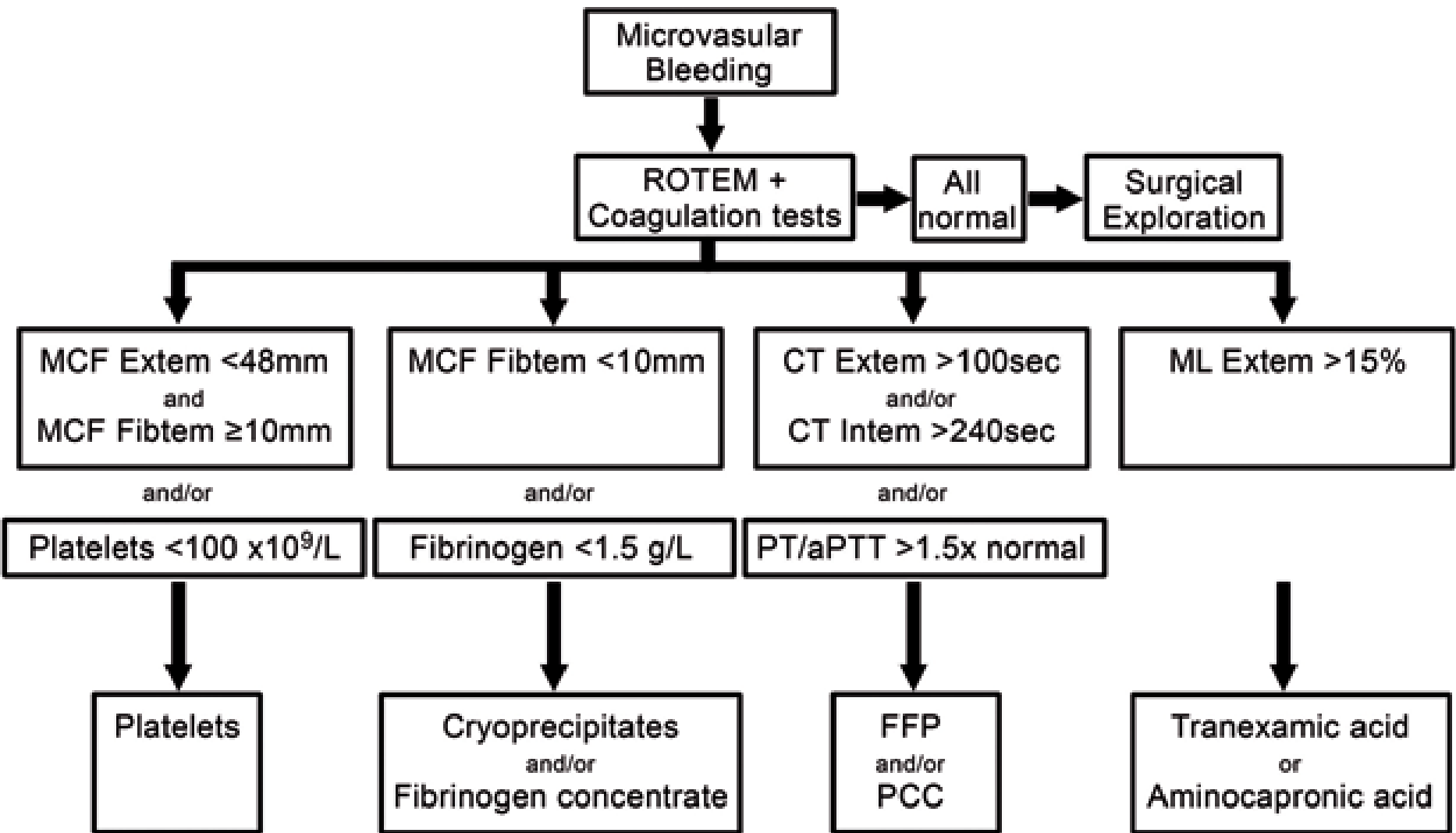
TxA benefit is related to the degree of shock.

CRASH-2  
Lancet 2010

# Thromboelastography (TEG / ROTEM)



# TEG/ROTEM guided transfusion resuscitation



# Massive Transfusion Consensus Conference

June 9-11, 2011 <http://mtcc2011.com/>

*Sheraton Centre Toronto Hotel*



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[Scribes](#) [Panel Login](#)

- International group of lecturers.
- Panel of 10 experts to forge consensus on 6 specific questions related to Trauma and Transfusion.
- Two reports:
  - Proceedings of the meeting
  - Panel responses to the questions