Massive Hemorrhage Protocol

Understanding what is needed to deliver high-quality, evidence-based care during a massive hemorrhage protocol activation

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Disclosures

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Outline

- Case
- Definitions and Goals of the MHP
- Core requirements and evidence
- Summary

Case

- 15 year old female child struck by pick-up truck while crossing the street at high speed
- Transported by land – injury to arrival time 23 minutes
- Patient receives 500 mL crystalloid in transport
- Team assembled prior to arrival in the emergency department and tasks assigned to each person by the physician lead
- Blood transfusion laboratory notified of incoming young female trauma and 4 units of unmatched O-negative, Kell-negative blood requested in a cooler

Case

- On arrival: obtunded, GCS 12, intubated immediately, HR 125, sBP 70 mmHg, temp 35.5°C
- Massive hemorrhage protocol activated
- Two RBC units started via rapid infuser blood warmer
- TXA 2 gram bolus given
- Two large bore catheters inserted and surgery resident assigned to insert central line
- Pupils unequal, 7 cm laceration to the back of the head with brisk bleeding
- Examination finds abdominal +FAST and concern for unstable pelvis

Case

- Labs drawn for group and screen, CBC, INR, PTT, fibrinogen, lytes, iCa, lactate
- Forced air blanket applied
- Persistent marked bleeding and hematoma from scalp injury despite pressure and staples
- Bleeding from central line puncture site
- Persistent hypotension despite 1 L Ringers and 2 RBC so 2 more RBC and 2 plasma being infused while awaiting lab testing
- Patient being prepared to go to CT scan

Case

- While patient in CT the following labs come back: Hb 115 g/L, platelet count 56 x 10^9/L, INR 5.4, fibrinogen 0.3 g/L
- You diagnose acute traumatic coagulopathy (likely severe due to traumatic brain injury) and transfuse 1 pool of platelets, 4 grams of fibrinogen, and 2 more plasma
- CT shows severe TBI with moderate subdural, splenic rupture and pelvic fracture
- Operating room is preparing for patient arrival
- Second set of labs drawn to determine status of coagulopathy and if additional fibrinogen/platelets/plasma are required


48
49

Massive Hemorrhage Protocol

A protocolized, multidisciplinary, and evidence-based approach to the management of the massively bleeding patient

Goals

- Activated promptly
- Right patient – not all bleeding patients need an MHP activation
- Activated through standardized communication process with distinct terminology
- Team promptly assembled and a team lead is designated
- First RBC spiked within 15 minutes
- Tranexamic acid given within 60 minutes (excluding gastrointestinal bleeds)
- Blood work at activation and every 60 minutes or every 4 RBCs
- Transfusion to target values, with 2:1 ratio until results available
- Avoid hypothermia
- Terminate when patient meets termination criteria
- Don’t waste blood

Callum JL, et al. CMAJ Open. 2019 Sep 3;7(3):E546-E561

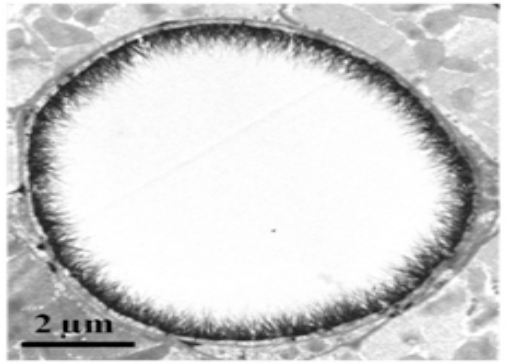
Definitions

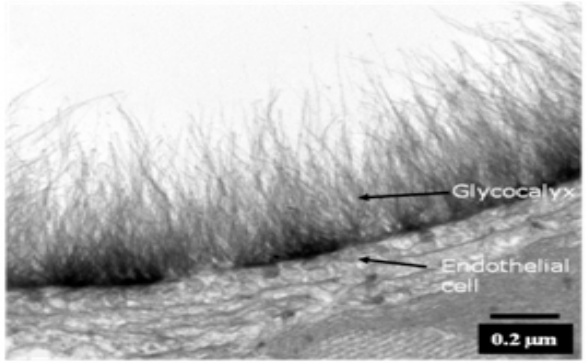
- Massive Transfusion = a retrospective definition used in clinical trials or observational studies to describe patients who were transfused a certain number (usually 10 U of RBC) in a 24 hour period

- Massive Hemorrhage Protocol (MHP) = a protocolized response to a massively bleeding patient (not all patients will end up receiving a massive transfusion)

Pathophysiology of trauma-associated coagulopathy

- Autoheparinization
- Upregulated thrombomodulin
- Activated protein C
- Depletion of factor V
- Uncontrolled tPA release
- Hyperfibrinolysis
- Activated endothelial cells
- Platelet dysfunction
- **Hypofibrinogenemia**





Other coagulation factors maintained

Duque P, Calvo A, Lockie C, Schöchl H. Pathophysiology of Trauma-Induced Coagulopathy. Transfus Med Rev. 2021 Oct;35(4):80-86.


Bleeding? <3 hrs from injury? Hemodynamically abnormal?
Consider Tranexamic Acid

1 Activate Promptly

- Every 1 minute delay from activation to first RBC is associated with a 5% increase in mortality

Multivariate regression predicting 30-day mortality

	Odds ratio	95% C.I.	p-value
Time to receipt of first cooler (min)	1.05	1.01–1.09	0.016
Anatomic injury severity (ISS)	1.05	1.03–1.06	<0.001
Disturbed arrival physiology (w-RTS)	0.61	0.53–0.69	<0.001
Randomization group (1:1:2)	1.46	0.92–2.29	0.102
Resuscitation Intensity (units)	1.03	0.60–1.44	0.184

680 patients from PROPPR study

Meyer DE, et al. Every minute counts: Time to delivery of initial massive transfusion cooler and its impact on mortality. J Trauma Acute Care Surg. 2017 Jul;83(1):19-24

Preventable delays in transfusion

- The UK Serious Hazards of Transfusion program put out an alert regarding delays in transfusion leading to preventable deaths:
  - 2010-2020: 809 reports to the haemovigilance system
  - There were 54 preventable deaths reported; accounting for 25% of all transfusion-related deaths

SHOT Serious Hazards of Transfusion

Preventing transfusion delays in bleeding and critically anaemic patients.

Date of Issue:	17-Jan-22	Reference No:	SHOT/2022/001
This alert is for action by: **NHS and independent (acute and specialist) sector where transfusions are carried out.**			
Access to blood components and products is a complex safety critical issue that is relevant across many departments and professions. Implementation of this alert should be coordinated by an executive leader (or equivalent role in organisations without executive boards) and supported by their designated senior leads for medical, nursing and pathology teams.			

Must have:

Protocols
Policies
Conduct drills
Investigate failures

https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103190

Maybe

Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock

Positive cluster trial

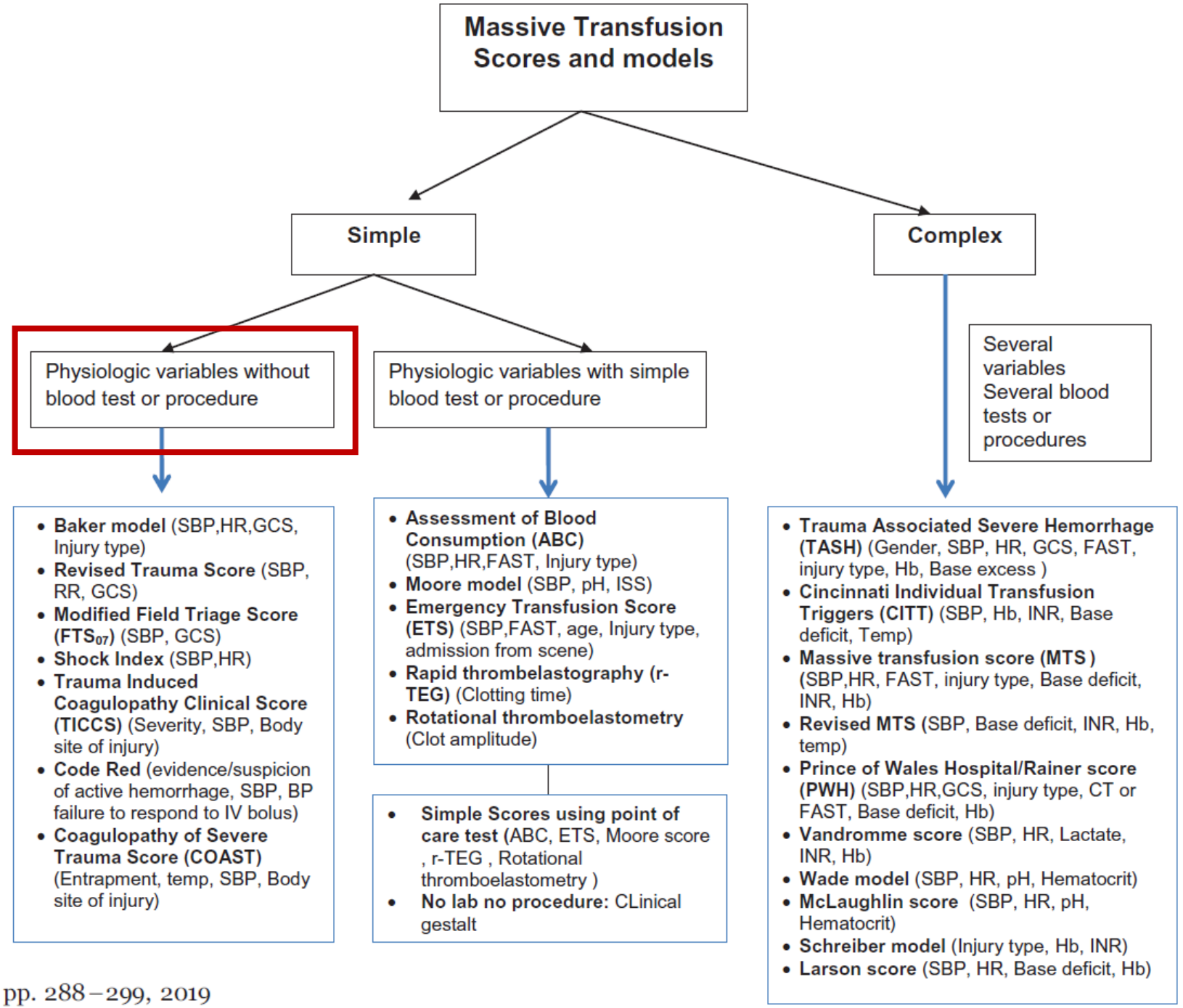
Pre-hospital transfusion		
	n	Findings
COMBAT	144	Prehospital plasma did not reduce mortality at 28-days when compared to normal saline
RePHILL	432	Pre-hospital red blood cells and lyophilized plasma did not improve patient outcomes when compared to normal saline
PREHO-PLYO	150	Pre-hospital plasma did not reduce INR levels, massive transfusion or 30-day mortality when compared to normal saline

2 Right kind of patient

Right mechanism ⇨
- High speed collision
- Penetrating trauma
- Post-partum hemorrhage

Bad hemodynamics ⇨
- High heart rate
- Low systolic blood pressure
- Needing inotropes
- Cardiac arrest
- Poor response to fluids

It would be better not to need lab tests



Clinician gestalt is no better either!

SHOCK, Vol. 52, No. 3, pp. 288–299, 2019

Shock Index triggers for MHP activation

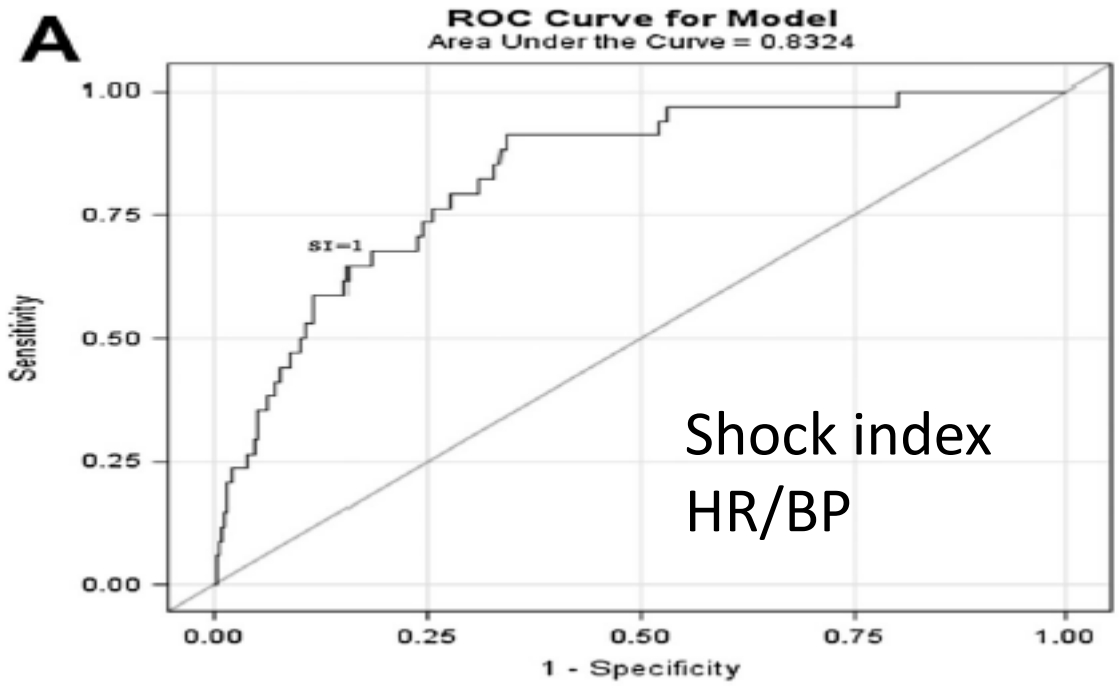
Heart Rate ÷ Systolic

> 1 → Obstetrics
Child (all ages)

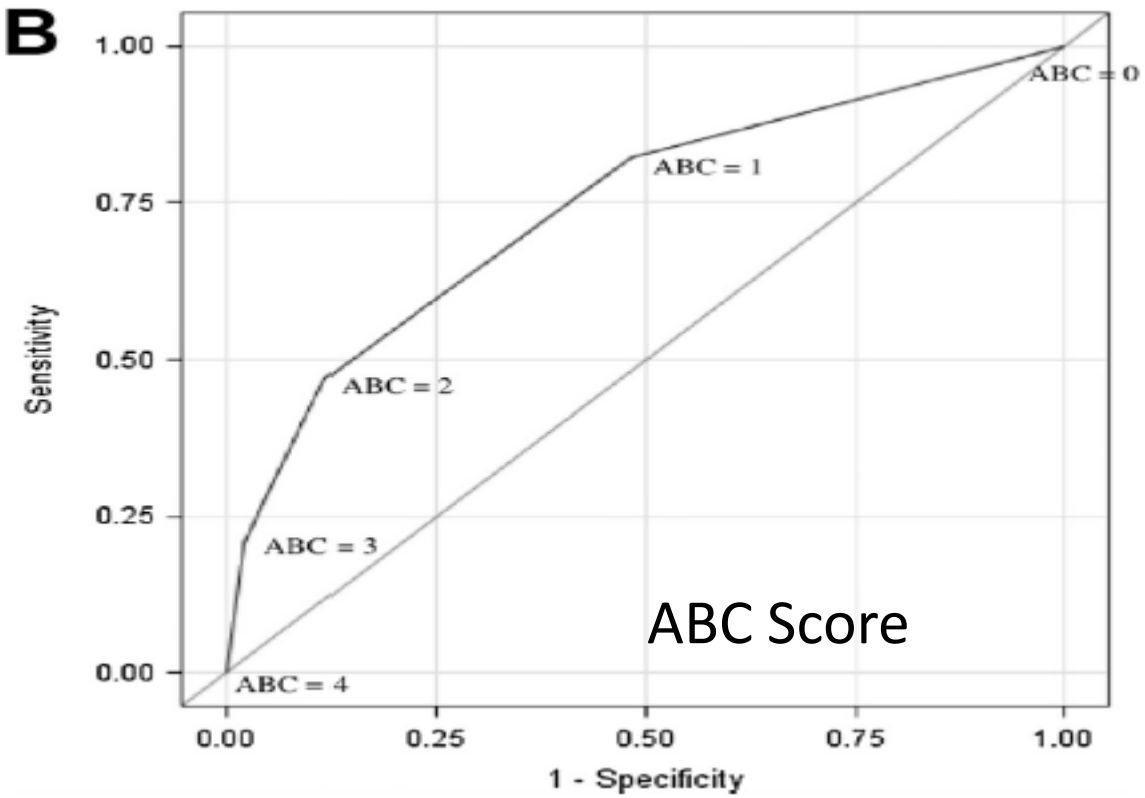
> 1.4 → Most patients

Schroll et al. Injury 2018 Jan;49(1):15-19

Shock Index vs ABC score to predict MT



SI≥1: Sens 68%, Spec 81%



ABC≥2: Sens 47%, Spec 89%

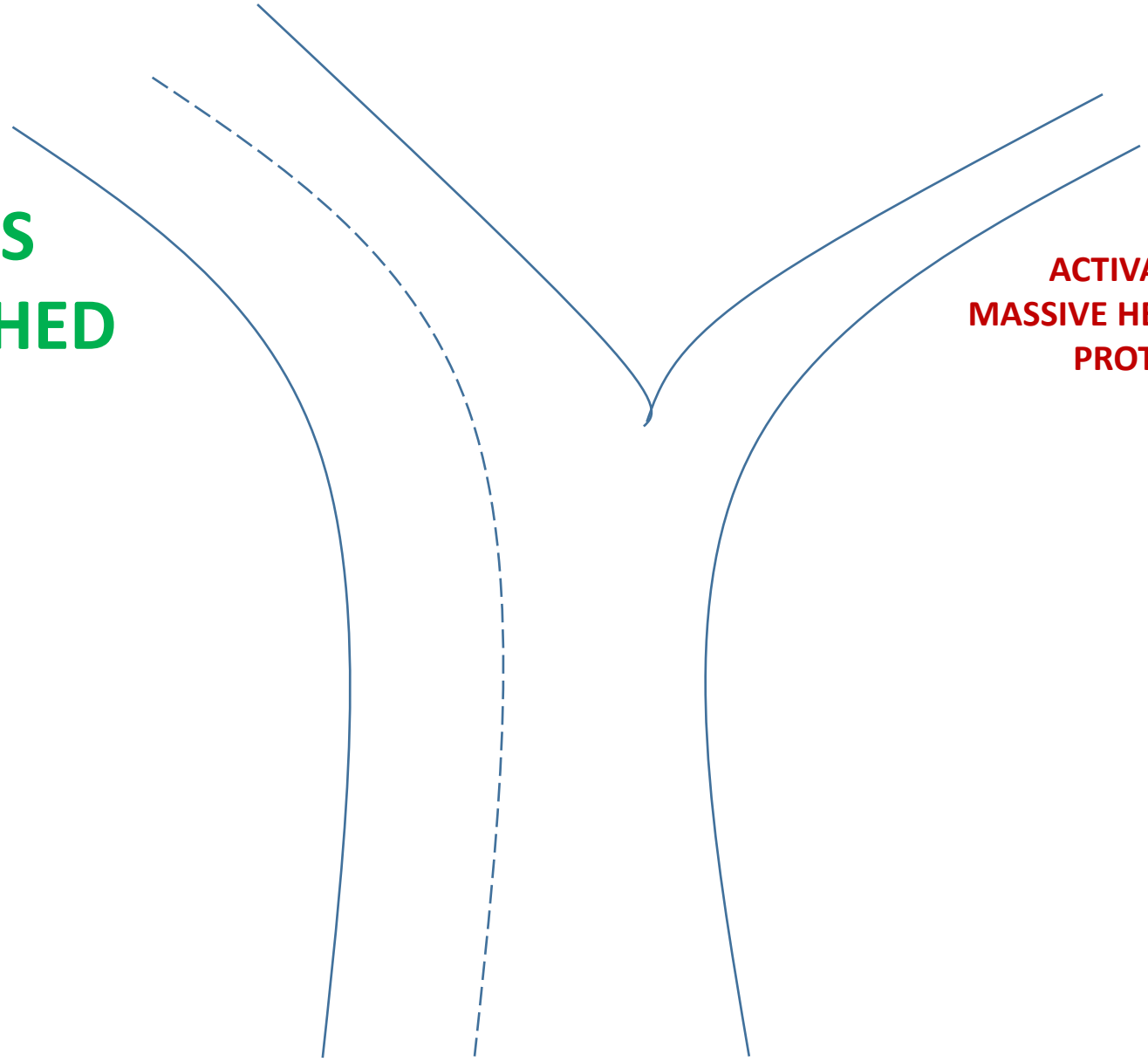
Schroll et al. Injury 2018 Jan;49(1):15-19

Do not activate the MHP to get uncrossmatched blood

- Just call blood bank for 2-4 units of uncrossmatched blood in a cooler
- The MHP is just for patients who will need at least 6 units of RBC and other components (plasma, platelets, fibrinogen concentrate/cryoprecipitate)

Callum JL, et al. CMAJ Open. 2019 Sep 3;7(3):E546-E561

4 UNITS UNMATCHED



ACTIVATE THE MASSIVE HEMORRHAGE PROTOCOL

Bleeding patient

GI Bleeds usually don’t usually need an MHP

In the GI bleeding trial called TRIGGER (n=936) performed in the UK, 95% of patients got just RBCs

[52 patients also excluded for “massive bleeding”]

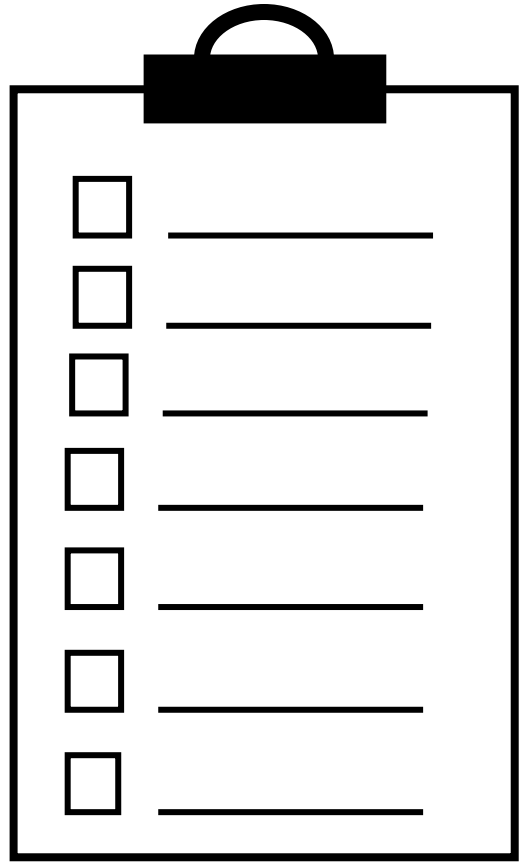
Jairath et al. TRIGGER. Lancet 2015;386(9989):137-44

You can still get plasma, platelets, fibrinogen replacement without activating the MHP

3 Activate the MHP via a planned Communications Pathway with distinct terminology

Here is how we do it at my hospital:

- Activated like a Code Blue
- Call 4444
- Say you are activating the Code Transfusion
- Stay on the line
- Blood Bank Tech will be conferenced in
- Answer the blood bank's questions so they know what to put in the blood coolers
- Code Transfusion will be announced overhead to alert hospital staff not to call blood bank except in emergencies
- Porter dispatched automatically



4 Team to assemble

- Designate lead physician
- Designate lead nurse for communication to porter, labs and other clinical staff
- Consider having an MHP phone that travels with the patient
- Repeated drills and simulations improve care

Brydges R, Hatala R, Zendejas B, et al. Linking simulation-based educational assessments and patient-related outcomes: a systematic review and meta-analysis. *Acad Med* 2015;90:246-56.
Gjeraa K, Moller TP, Ostergaard D. Efficacy of simulation-based trauma team training of non-technical skills. A systematic review. *Acta Anaesthesiol Scand* 2014;58:775-87.

5 Commence transfusion promptly with a minimum ratio of 2:1 RBC: plasma

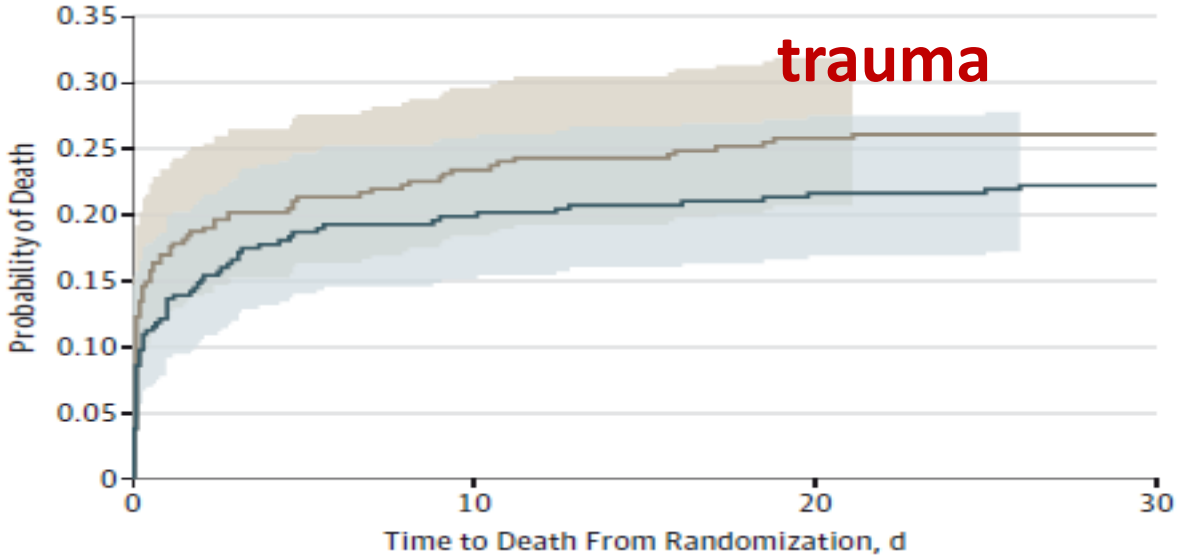
e.g.

Box 1	Box 2	Box 3	Box 4+
4 units of RBC	4 units of RBC 4 units of Plasma	4 units of RBC 2 units of Plasma 4 grams fibrinogen	4 units of RBC 2 units of Plasma

- Other items can be ordered as needed “à la carte” (e.g. more platelets, PCC, or fibrinogen)
- Pediatric weight based coolers for kids

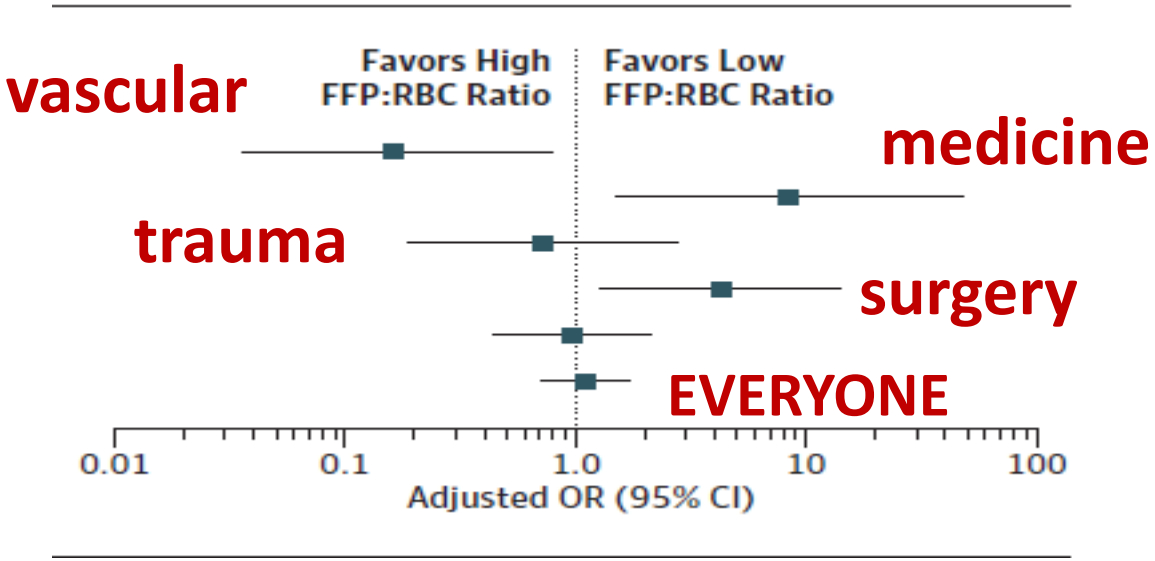
1:1 = 2:1

PROPRR



Holcomb, JAMA 2015; 313: 471-482

JAMA SURG HARVARD



Mesar, JAMA Surg 2017; March 8.

Guidelines recommend 2:1

GUIDELINES

Transfusion strategies in bleeding critically ill adults: a clinical practice guideline from the European Society of Intensive Care Medicine

Alexander P. J. Vlaar[1*], Joanna C. Dionne[2,3,4,21], Sanne de Bruin[1], Marije Wijnberge[1,5], S. Jorinde Raasveld[1], Frank E. H. P. van Baarle[1], Massimo Antonelli[6,7], Cecile Aubron[8], Jacques Duranteau[9], Nicole P. Juffermans[10,11], Jens Meier[12], Gavin J. Murphy[13], Riccardo Abbasciano[13], Marcella C. A. Müller[1], Marcus Lance[14], Nathan D. Nielsen[15], Herbert Schöchl[16,17], Beverley J. Hunt[18], Maurizio Cecconi[19,20] and Simon Oczkowski[2,3,4]

Intensive Care Med (2021) 47:1368–1392
https://doi.org/10.1007/s00134-021-06531-x

Recommendation

We **suggest** use of high-ratio transfusion strategies (at least one unit plasma per two units of packed red blood cells) vs. low-ratio transfusion strategies in critically ill patients with massive bleeding due to trauma (*Conditional recommendation, low certainty of evidence*).

GUIDELINE

Haematological management of major haemorrhage: a British Society for Haematology Guideline

Simon J. Stanworth[1,2,3] | Kerry Dowling[4] | Nikki Curry[2,3] | Heidi Doughty[5,6] | Beverley J. Hunt[7] | Laura Fraser[8,9] | Shruthi Narayan[10] | Juliet Smith[11] | Ian Sullivan[12] | Laura Green[13,14,15] | The Transfusion Task Force of the British Society for Haematology

- If major bleeding is on-going and results of standard coagulation tests or near-patient tests are not available, we suggest that units of FFP be transfused in at least a 1:2 ratio with units of RBCs. (2B)

Br J Haematol. 2022;198:654–667.

GUIDELINES **Open Access**

The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition

Rolf Rossaint[1*], Arash Afshari[2], Bertil Bouillon[3], Vladimir Cerny[4,5], Diana Cimpoesu[6], Nicola Curry[7,8], Jacques Duranteau[9], Daniela Filipescu[10], Oliver Grottke[1], Lars Grønlykke[11], Anatole Harrois[9], Beverley J. Hunt[12], Alexander Kaserer[13], Radko Komadina[14], Mikkel Herold Madsen[2], Marc Maegele[15], Lidia Mora[16], Louis Riddez[17], Carolina S. Romero[18], Charles-Marc Samama[19], Jean-Louis Vincent[20], Sebastian Wiberg[11] and Donat R. Spahn[13]

Initial coagulation resuscitation

Recommendation 25 In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies:

- Fibrinogen concentrate or cryoprecipitate and pRBC (Grade 1C)
- FFP or pathogen-inactivated FFP in a FFP/pRBC ratio of at least 1:2 as needed (Grade 1C)

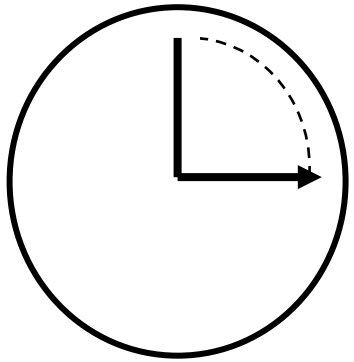
Rossaint *et al. Critical Care* (2023) 27:80
https://doi.org/10.1186/s13054-023-04327-7

Note on divisive language

- “pasta water”
- “unbalanced resuscitation”
- “if they are bleeding blood, they need blood”

6 Give Tranexamic acid within 60 minutes

- Every 15 minute delay to tranexamic acid is associated with a 10% drop in survival benefit



Guyette FX, et al. JAMA Surg. 2020 Oct 5;156(1):11–20
Shakur H, et al. *Lancet.* 2010; 376:23-32
Gayet-Ageron A, et al. Lancet. 2018 Jan 13;391(10116):125-132

Tranexamic acid evidence

- Key trials:
  - CRASH-2 in 20,211 trauma patients
  - MATTERS in 896 military trauma patients
  - STAAMP in 927 pre-hospital trauma patients
  - CRASH-3 in 12,737 trauma patients with TBI
  - ROC-TXA in 1,280 pre-hospital trauma patients with TBI

Safe
Reduces mortality
Optimal <60 minutes

Shakur H, et al. *Lancet.* 2010; 376:23-32
Morrison et al. Arch Surg 2012;147:113-9
Guyette FX, et al. JAMA Surg. 2020 Oct 5;156(1):11–20
CRASH-3 trial collaborators. Lancet. 2019;394:1713-1723
Rowell SE, et al. JAMA. 2020 Sep 8;324(10):961-974

Systematic review – thromboembolic complications

Cause of death	No. of studies	Events in TXA group	Events in Control group	OR (95%CI)	P value	I^2 statistic
Myocardial infarction	5	45/11,288 (0.4%)	64/10,982 (0.6%)	0.66 (0.45, 0.97)	0.03	0%
Stroke	5	73/11,288 0.6%)	76/10,982 (0.7%)	0.90 (0.65, 1.24)	0.50	40%
Thromboembolic events	6	67/1,308 (5.1%)	62/963 (6.4%)	0.89 (0.37, 2.11)	0.79	60%
Pulmonary embolism	5	137/12,112 (1.1%)	117/13,800 (0.8%)	1.57 (0.79, 3.13)	0.20	80%
Deep vein thrombosis	6	105/12,240 (0.9%)	105/13,925 (0.8%)	1.13 (0.51, 2.51)	0.77	83%

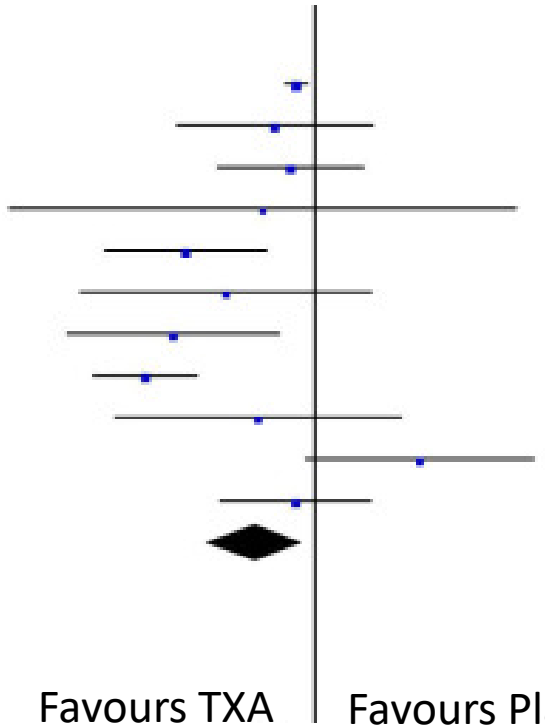
Al-Jeabory M, et al. J Clin Med. 2021 Mar 3;10(5):1030.

Systematic review (Mortality, Trauma)

b Civil use						
CRASH-2 2010 [36]	1463	10060	1613	10067	11.4%	0.89 [0.83, 0.96]
El-Menyar 2020 [25]	25	102	30	102	7.1%	0.78 [0.42, 1.45]
Guyette 2020 [26]	37	447	43	453	8.6%	0.86 [0.54, 1.36]
Kakaei 2017 [28]	3	30	4	30	2.3%	0.72 [0.15, 3.54]
Myers 2019 [31]	136	189	161	189	8.1%	0.45 [0.27, 0.74]
Neeki 2017 [32]	8	128	13	125	4.9%	0.57 [0.23, 1.44]
Neeki 2018 [33]	13	362	30	362	6.7%	0.41 [0.21, 0.80]
Rivas 2021 [35]	106	654	91	254	9.8%	0.35 [0.25, 0.48]
Swendsen 2013 [37]	9	52	17	74	5.0%	0.70 [0.29, 1.73]
Valle 2014 [38]	25	109	14	105	6.3%	1.93 [0.94, 3.97]
Wafaisade 2016 [39]	38	258	42	258	8.4%	0.89 [0.55, 1.43]
Subtotal (95% CI)		**12391**		**12019**	**78.7%**	**0.69 [0.51, 0.93]**
Total events	1863		2058			

Heterogeneity: $Tau^2 = 0.16$; $Chi^2 = 46.34$, df = 10 ($P < 0.00001$); $I^2 = 78\%$

Test for overall effect: $Z = 2.41$ ($P = 0.02$)



Al-Jeabory M, et al. J Clin Med. 2021 Mar 3;10(5):1030

CRASH-3 plus ROC-TXA in traumatic brain injury

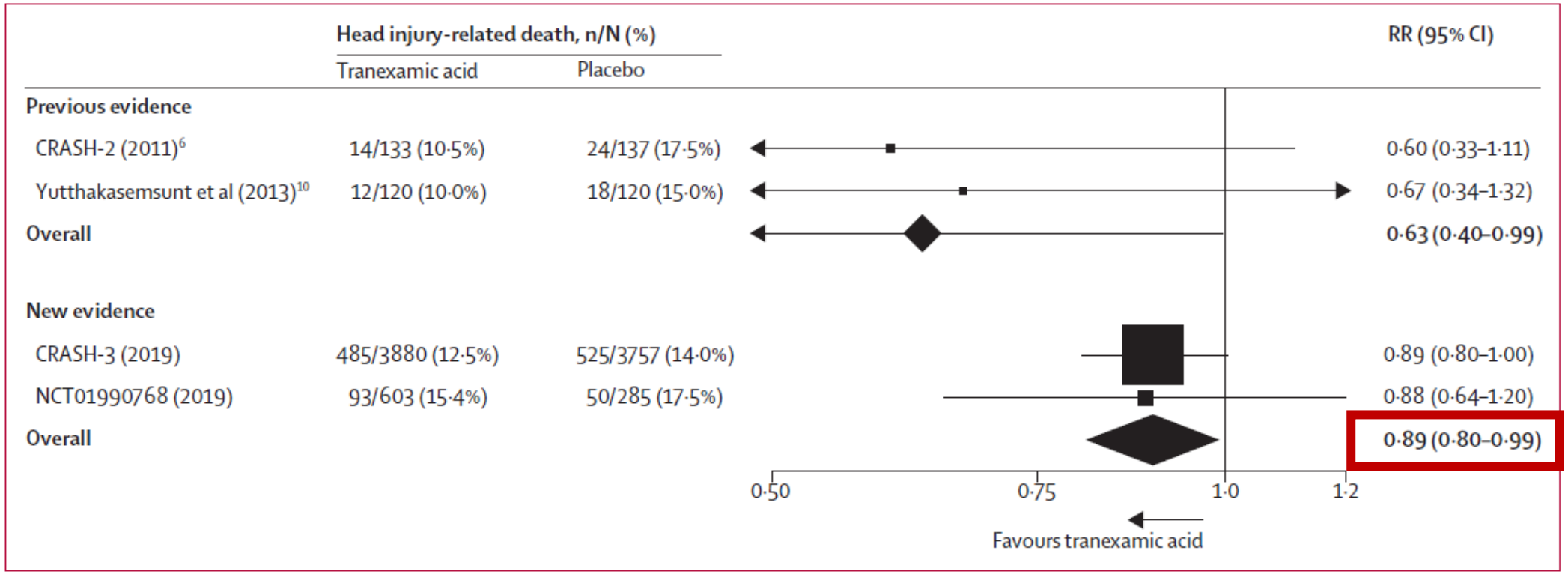


Figure 5: Evidence on the effect of tranexamic acid on head injury-related death
RR=risk ratio.

Lancet 2019; 394: 1713–23

TXA improves the coagulopathy

Table 3. Changes of Laboratory and ROTEM Values Between On-Scene and the ED

	Changes From On-Scene to ED Admission		Difference Between TXA and C	
	C, n = 24 Mean [SD]	TXA, n = 24 Mean [SD]	Difference in Means (95% CI)	*P* Value
pH	0.00 [0.07]	0.02 [0.09]	−0.02 (−0.07 to 0.03)	.43
Standard bicarbonate (mmol/L)	−0.3 [2.6]	−1.4 [2.8]	1.1 (−0.5 to 2.6)	.21
Base excess	−0.3 [2.3]	−0.8 [2.1]	0.5 (−0.8 to 1.8)	.90
Anion gap (mmol/L)	−0.9 [3.1]	−2.4 [3.1]	1.5 (−0.3 to 3.3)	.13
Hemoglobin (g/L)	−21 [27]	−25 [19]	4 (−10 to 18)	.28
Lactate (mmol/L)	−0.6 [1.3]	−1.2 [1.1]	0.6 (−0.1 to 1.3)	.03
EXTEM MCF (mm)	−8.2 [4.1]	1.0 [2.5]	−9.2 (−11.2 to −7.2)	**<.001**
EXTEM ML (%)	0 [4]	−12 [27]	12 (1–24)	**<.001**
INTEM MCF (mm)	−7.7 [4.5]	−0.8 [2.7]	−6.8 (−9.0 to −4.7)	**<.001**
INTEM ML (%)	−2 [16]	−11 [20]	9 (−3 to 22)	**<.001**
FIBTEM MCF (mm)	−3.7 [1.8]	−0.2 [2.8]	−3.5 (−4.8 to −2.1)	**<.001**
FIBTEM ML (%)	−1 [22]	−4 [31]	3 (−12 to 19)	.08
Quick's value (%)	2 [16]	−6 [17]	7 (−2 to 17)	.14
INR	0.0 [0.1]	0.0 [0.2]	−0.1 (−0.2 to 0.0)	.26
Fibrinogen (g/L)	−0.4 [0.5]	−0.5 [0.5]	0.1 (−0.2 to 0.4)	.41
Factor XIII activity (%)	−18 [18]	−17 [21]	−1 (−12 to 11)	.85
Factor V activity (%)	−15 [23]	−18 [17]	3 (−9 to 14)	.51
D-dimers (mg/dL)	3.9 [5.4]	0.1 [2.2]	3.9 (1.5 to 6.3)	**.002**
Protein C activity (%)	−13 [18]	−11 [16]	−2 (−12 to 8)	.58

Stein P, et al. Anesth Analg. 2018 Feb;126(2):522-529.

WOMAN Trial (n=20,060)

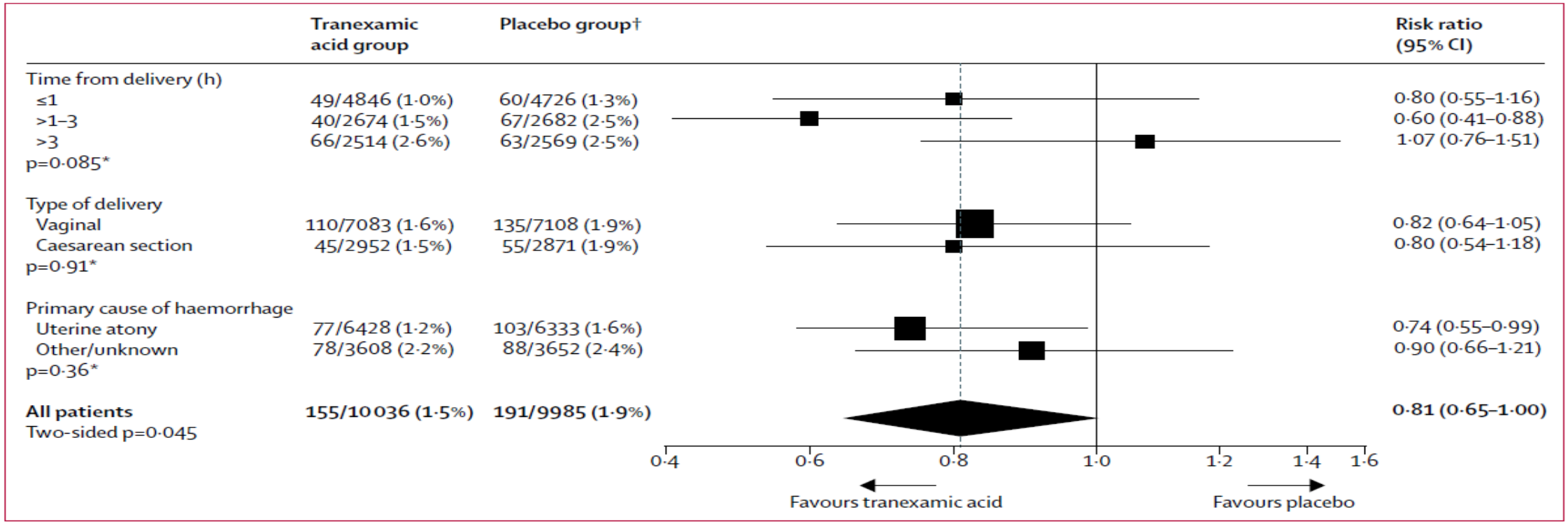


Figure 3: **Death from bleeding by subgroup**

*Heterogeneity p value. †One patient excluded from subgroup analysis because of missing baseline data.

Published online April 26, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30638-4

Tranexamic acid

- Give 2 grams for all adults
  - 2 grams as a bolus/infusion
  - Or give 2 x 1 gram iv pushes one hour apart
  - Or if you are very sophisticated 1 gram bolus plus 1 gram infusion
  - [kids: 15mg/kg IV bolus then 5mg/kg/hr IV infusion for 8 hours, to a maximum total dose of 2 grams]
- Don’t bother if more than 3 hours from injury/bleed – no residual benefit
- [Don’t give to GI bleeds – it doesn’t work and causes more clots]

J Emerg Crit Care Med 2021;5:15 | http://dx.doi.org/10.21037/jeccm-20-108

Shakur H, et al. *Lancet.* 2010; 376:23-32
HALT-IT Trial Collaborators. Lancet. 2020 Jun 20;395(10241):1927-1936

ROC-TXA infusion rate

5.2.7 Justification for dose selection

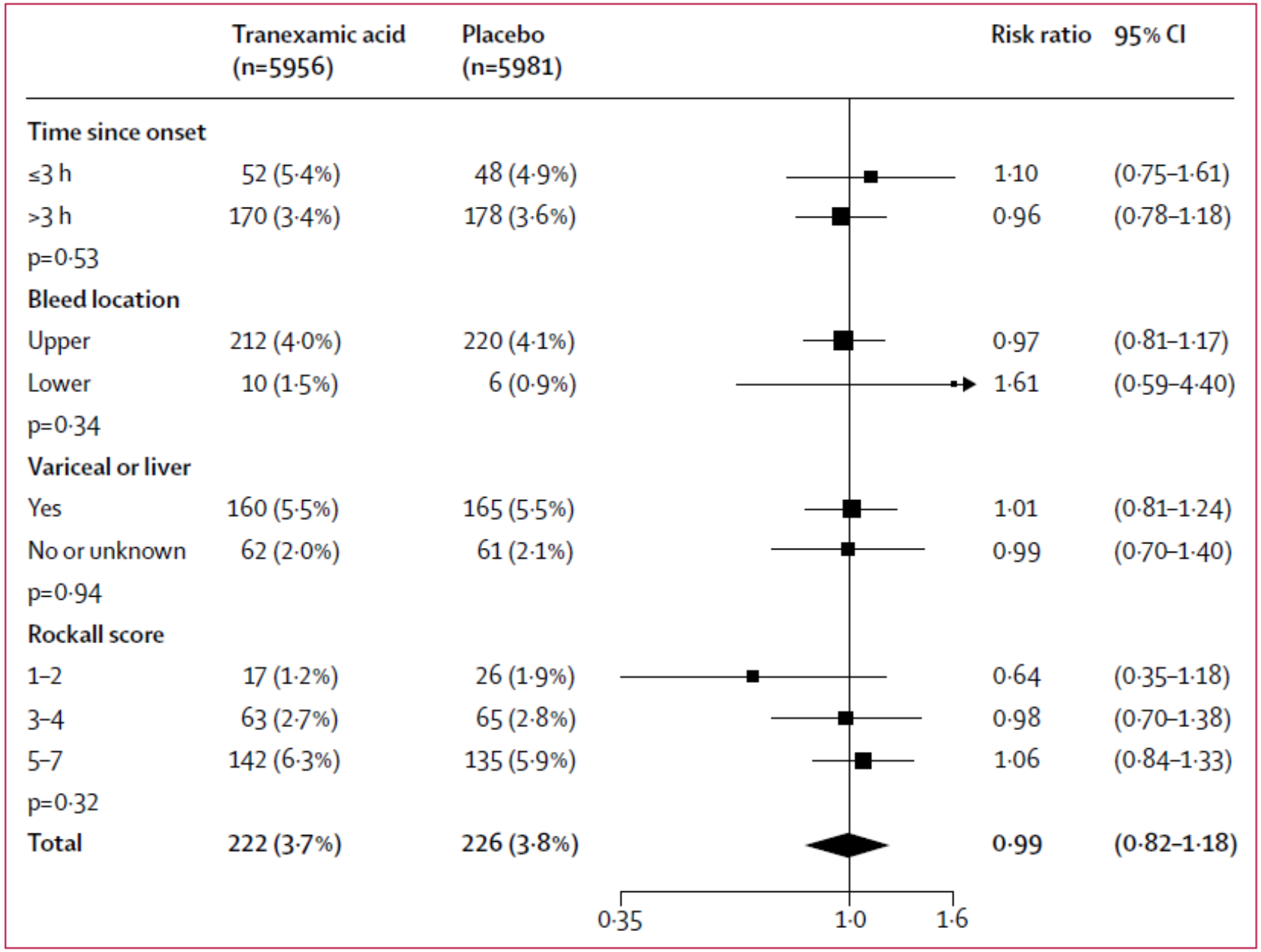
The dose selection for the study drug is as follows:

- *Bolus/maintenance arm*: 1 gram IV TXA in 250 mL administered wide open followed by a 1 gram maintenance IV TXA infusion over 8 hours (weight based equivalent: 50 kg person – bolus 20 mg/kg, maintenance 2.5 mg/kg/h; 75 kg person – bolus 13.3 mg/kg, maintenance 1.7 mg/kg/h; 100 kg person – bolus 10 mg/kg, maintenance 1.25 mg/kg/h)
- *Bolus only arm*: 2 grams IV TXA in 250 mL administered wide open followed by a maintenance placebo infusion over 8 hours (weight based equivalent: 50 kg person – bolus 40 mg/kg; 75 kg person – 26.7 mg/kg bolus; 100 kg person – bolus 20 mg/kg)

Rowell SE, et al. JAMA. 2020 Sep 8;324(10):961-974.

HALT-IT

HALT-IT Trial Collaborators. Lancet. 2020 Jun 20;395(10241):1927-1936.



	Tranexamic acid (n=5956)	Placebo (n=5981)	Risk ratio	95% CI
Time since onset				
≤3 h	52 (5·4%)	48 (4·9%)	1·10	(0·75–1·61)
>3 h	170 (3·4%)	178 (3·6%)	0·96	(0·78–1·18)
p=0·53				
Bleed location				
Upper	212 (4·0%)	220 (4·1%)	0·97	(0·81–1·17)
Lower	10 (1·5%)	6 (0·9%)	1·61	(0·59–4·40)
p=0·34				
Variceal or liver				
Yes	160 (5·5%)	165 (5·5%)	1·01	(0·81–1·24)
No or unknown	62 (2·0%)	61 (2·1%)	0·99	(0·70–1·40)
p=0·94				
Rockall score				
1–2	17 (1·2%)	26 (1·9%)	0·64	(0·35–1·18)
3–4	63 (2·7%)	65 (2·8%)	0·98	(0·70–1·38)
5–7	142 (6·3%)	135 (5·9%)	1·06	(0·84–1·33)
p=0·32				
Total	222 (3·7%)	226 (3·8%)	0·99	(0·82–1·18)

0·35 1·0 1·6

Figure 3: Effect of tranexamic acid on death due to bleeding within 5 days

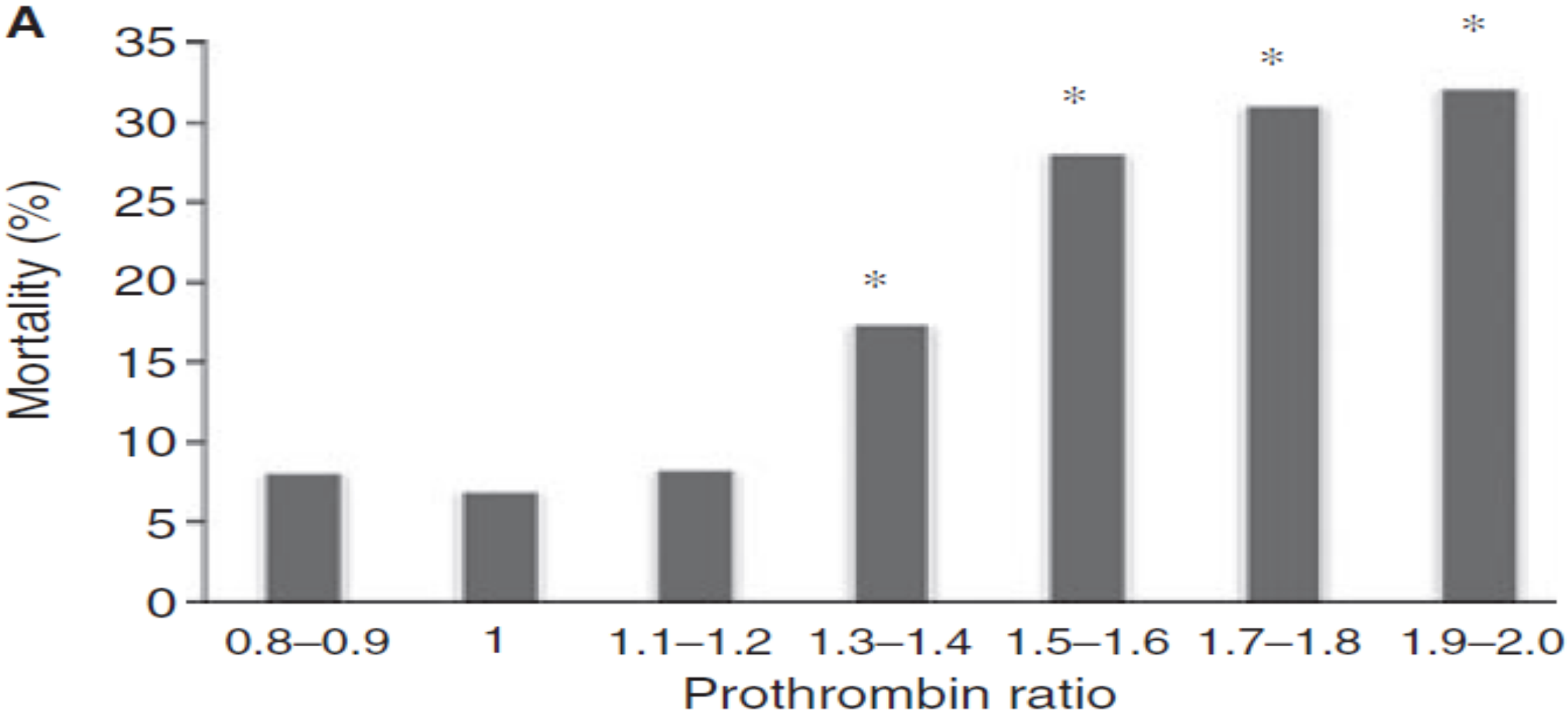
7 Blood work at activation and hourly

- Baseline:
  - **BLOOD GROUP AND SCREEN**
  - CBC, INR, PTT, fibrinogen
  - Electrolytes, ionized Ca, lactate
- Hourly or q4 units RBC:
  - CBC, INR, fibrinogen (no need to do hourly PTT if baseline concordant with INR)
  - K+, ionized Ca++ for monitoring for transfusion toxicity and lactate
- Ensure your lab calls back ALL hematology results and critical chemistry results

Use order groups in your EMR so you don’t miss doing a test

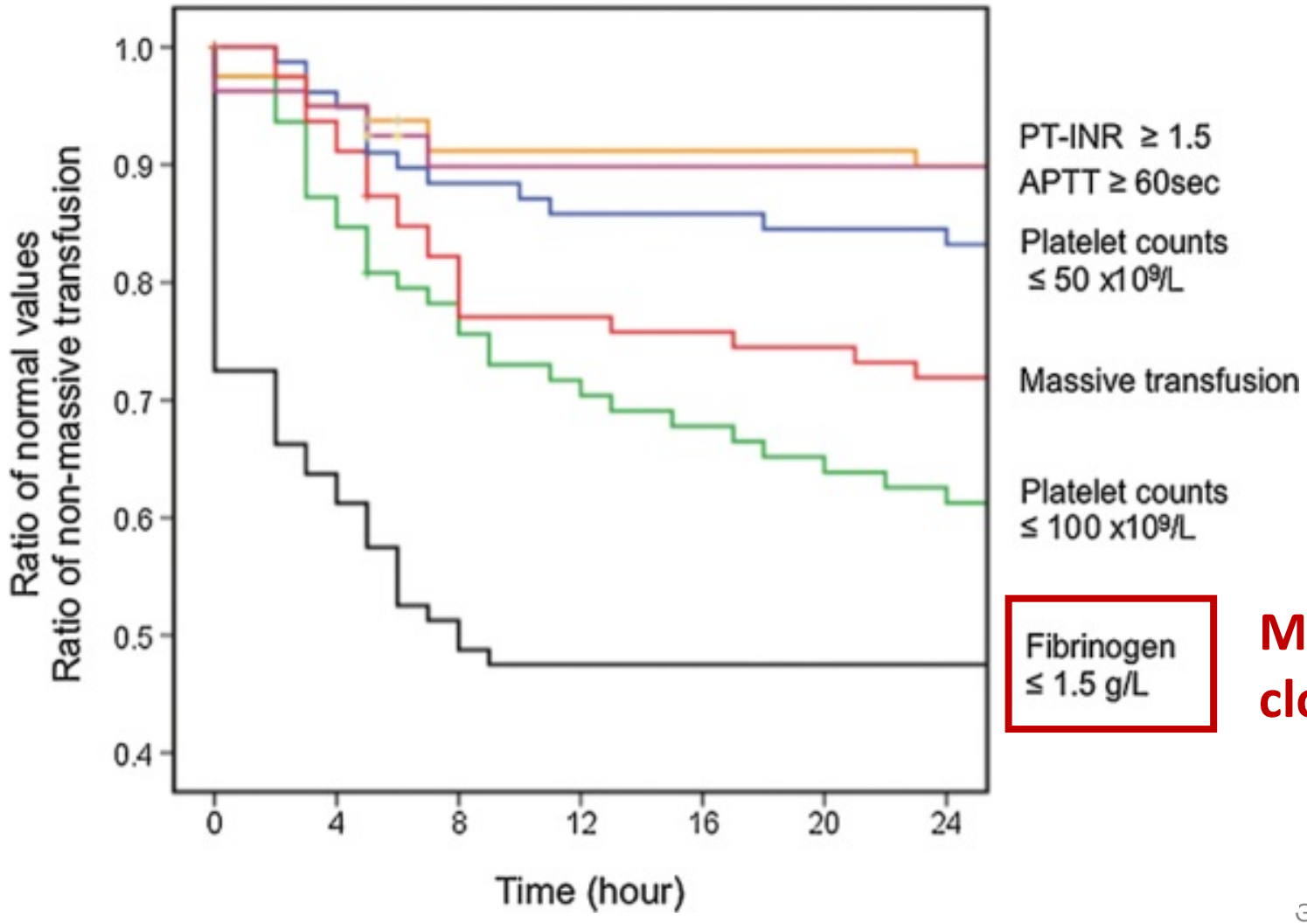
Mortality increases at >1.2

Firth D, et al. J H and T 2010; 8: 1919-25



Baseline INR tells you how badly injured your patient is

Time from arrival in ED to critical levels



Monitor fibrinogen closely

Gando & Hayakawa 2016

Two ways to test

INR, PTT, and fibrinogen done in the laboratory on a centrifuged plasma sample

vs.

Viscoelastic testing

ROTEM impact - Cardiac Surgery-related Hemorrhage Step-wedge cluster RCT (7402 patients)

Outcome	Relative Risk (95% CI)	P-value
Red cell transfusions	**0.91 (0.84, 0.98)**	**0.01**
Platelet transfusions	**0.81 (0.72, 0.91)**	**<0.001**
Plasma transfusions	1.04 (0.91, 1.18)	0.57
Cryoprecipitate or fibrinogen concentrate transfusions	1.19 (0.89, 1.59)	0.24
Major bleeding	**0.86 (0.75, 0.98)**	**0.02**
Major complications	1.01 (0.80, 1.26)	0.97

Karkouti et al. Circulation. 2016;1341152-1162

iTACTIC Trial (n=396) – TEG/ROTEM vs conventional clotting assays

Table 2 Secondary outcomes for the intention-to-treat population

	CCT (*n* = 195)	VHA (*n* = 201)	Odds ratio (95% CI)	*p* value
Mortality at 6 h—no. (%)	22/195 (11%)	22/201 (11%)	0.97 (0.52–1.80)	0.915
Mortality at 24 h—no. (%)	33/195 (17%)	29/201 (14%)	0.83 (0.48–1.42)	0.495
Mortality at 28 days—no. (%)	55/194 (28%)	50/201 (25%)	0.84 (0.54–1.31)	0.435
Mortality at 90 days—no. (%)	56/177 (31%)	53/179 (29%)	0.91 (0.58–1.42)	0.678
Death from exsanguination—no. (%)	17/56 (30%)	13/51 (25%)	0.78 (0.34–1.82)	0.576
Died before haemostasis—no. (%)	24/54 (44%)	19/50 (38%)	0.77 (0.35–1.67)	0.505

TEG/ROTEM patients 1.8-times more likely to get non-RBC products

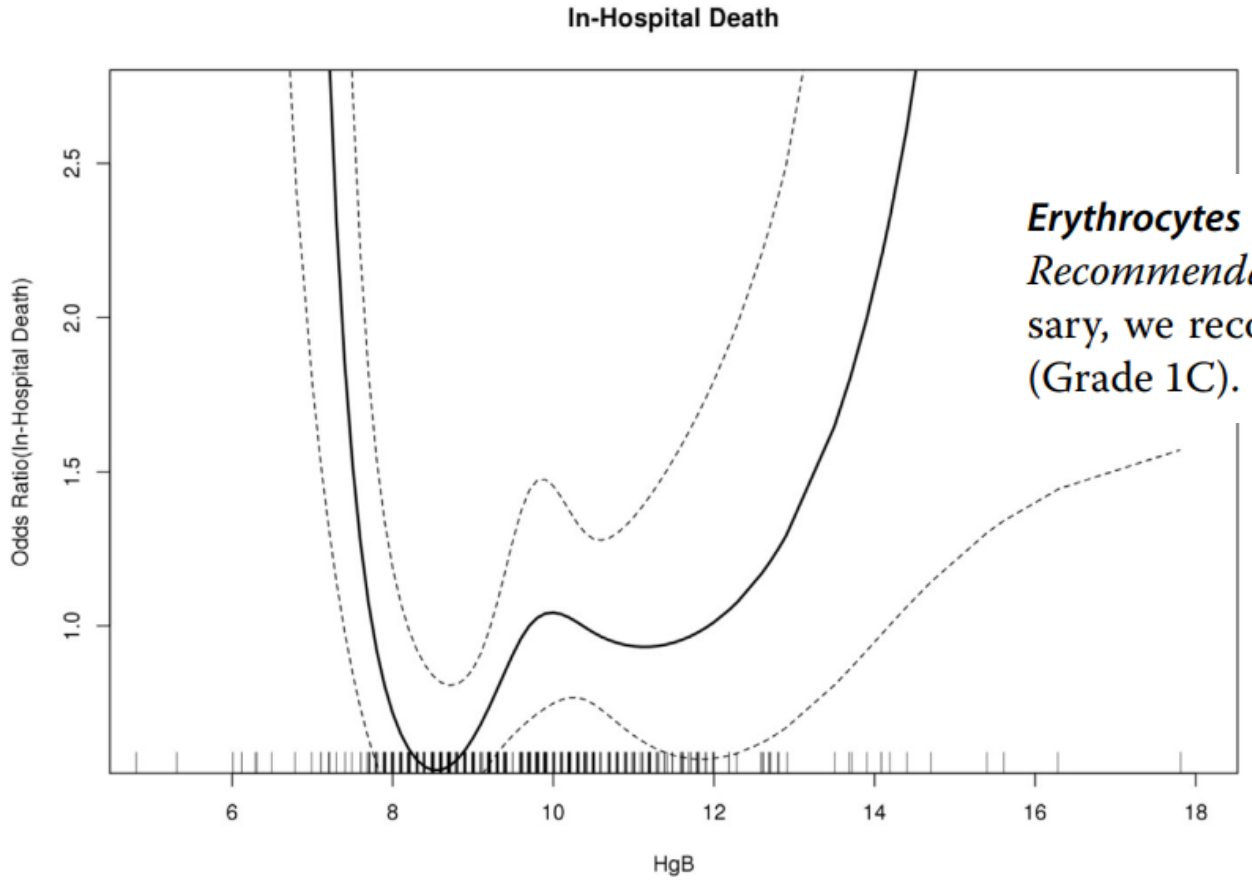
Baksaas-Aasen K, Gall LS, Intensive Care Med. 2021 Jan;47(1):49-59.

8 Transfuse to Target

BEWARE: Just because you are giving ratio-based resuscitation doesn't mean you will stay on target. Formula-based ratios are just for initial care.

Lab metric	Target
Hemoglobin	60-110 g/L Keep over 80 g/L if possible
Platelet count	Keep over 50 (over 100 for cardiac surgery and head trauma)
INR	Keep below 1.8 (or use similar cut off with viscoelastic testing, e.g. ROTEM CT>90 seconds)
Fibrinogen	Keep over 1.5 g/L (over 2.0 g/L for cardiac and obstetrics) (or use similar cut off with viscoelastic testing, e.g., FIBTEM<8-10)

Under and over transfusion are bad



Erythrocytes

Recommendation 16 If erythrocyte transfusion is necessary, we recommend a target haemoglobin of 70–90 g/L (Grade 1C).

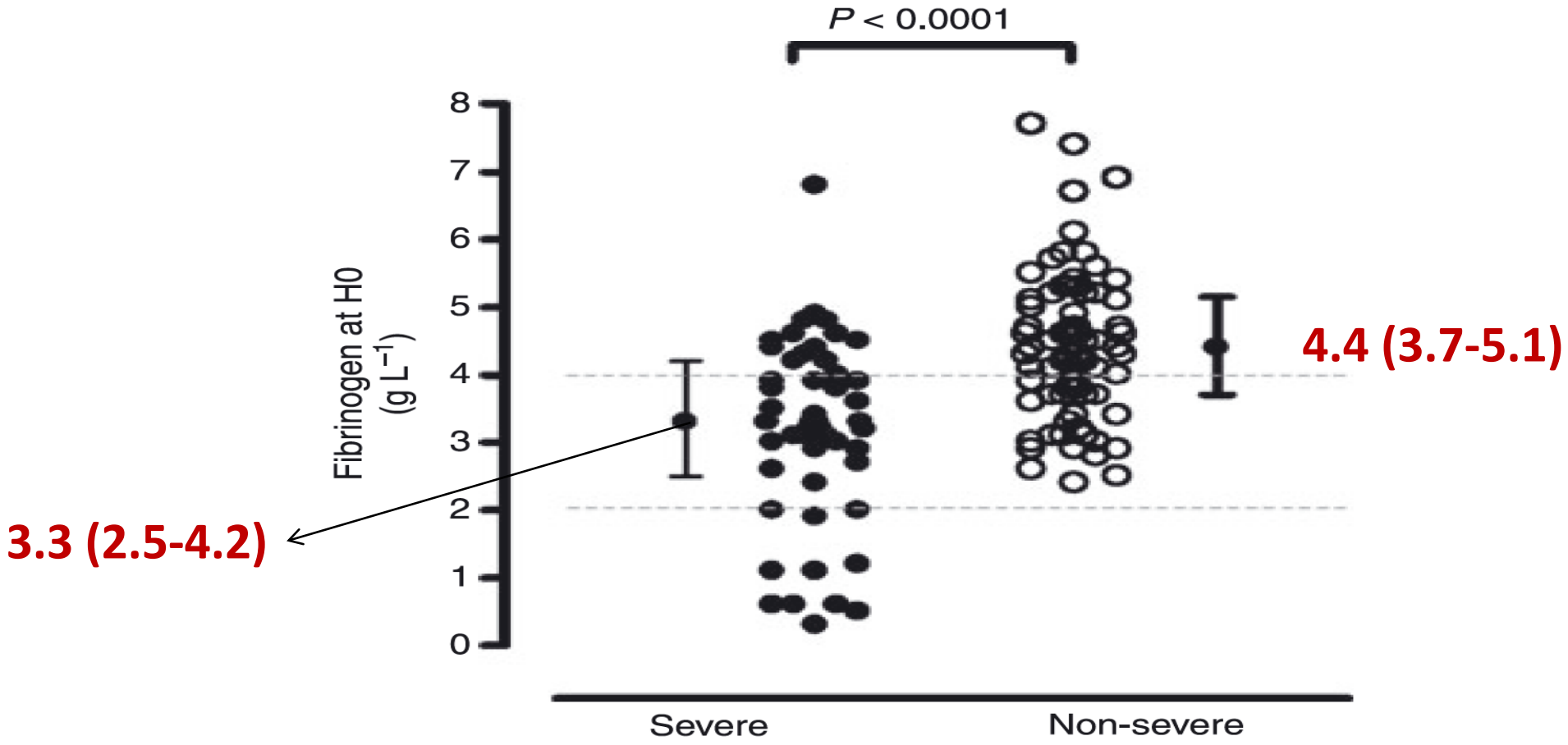
Rossaint *et al. Critical Care* *(2023) 27:80*
https://doi.org/10.1186/s13054-023-04327-7

Fig 1. The odds of death (Y-axis) based on the hemoglobin (HgB) value 24 ± 6 hours after anatomic hemostasis (X-axis). The odds of death are controlled for age, sex, and Charlson Comorbidity Score. The inflection points for increased mortality odds were >12.0 g/dL (pRBc overtransfusion) and <8.0 g/dL (undertransfusion). The ideal HgB range was defined as 8.0–12.0 g/dL.

Zielinski MD, et al. Surgery. 2016 Dec;160(6):1560-1567

Fibrinogen<2.0 g/L and PPH

[Pregnant patients without bleeding have fibrinogens between 3.5-6.5]



Charbit, et al. JHT 2006; 5: 266-73

Reverse anticoagulants

REVERSE ANTICOAGULANTS

Warfarin
IV Vitamin K 10 mg
INR 1.5 to 3.0 – 1000 IU PCC
INR 3.0 to 5.0 – 2000 IU PCC
INR > 5.0 - 3000 IU PCC
Unknown INR – 2000 IU PCC

Dabigatran - Idarucizumab (Praxbind) 5 g IV

Xa Inhibitors - PCC 2000 IU
Repeat at 1 hour if ongoing hemorrhage

In some jurisdictions Andexanet alpha available

9 Avoid hypothermia

- Keep temperature over 36°C
- Use blood warmer for all fluids
- Use active warming blankets
- Monitor temperature every 30 minutes

https://www.bairhugger.com/3M/en_CA/bair-hugger-ca/

https://belmontmedtech.com/rapid-infusion-pump

Hypothermia – Prevention & Management

- Minimal number of studies
- Poorly monitored during pre-hospital and pre-OR phase
- Temp <34°C associated with an increase in mortality
- Each 1°C increases blood loss by 16% and risk of transfusion by 22%
- In the pre-hospital phase, trauma patients with minor injury have a fall in temperature with passive warming (blankets), versus a rise with resistive warming blankets AND they are more comfortable on arrival

Reynolds BR, et al. J Trauma Acute Care Surg. 2012; **73**(2): 486-91.
Dirkmann D, et al. Anesth Analg. 2008; **106**(6): 1627-32.
Kober A, et al. Mayo Clin Proc. 2001; **76**(4): 369-75.
Walpoth BH, et al. N Engl J Med. 1997; **337**(21): 1500-5.
Lundgren P, et al. Scand J Trauma Resusc Emerg Med. 2011; **19**: 59.

10 Termination procedure

- Terminate when hemorrhage control is achieved, hemodynamics improving, coagulation parameters improving, and rate of transfusion has slowed
- Call blood bank or designated communication route to terminate
- Return unused blood to blood bank immediately
- Bedside debrief – talk about what the team did well and what did not go well – learn from your mistakes

11 Don’t waste blood

- Keep the blood packed exactly as it comes from the blood bank
- Do not move blood from one cooler to another
- Don’t put empties in your cooler – they contaminate the other units and if not used, have to be discarded
- Don’t write on the unit labels – if you do they have to be discarded
- Return as soon as identified the products are not needed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1	Triggering
2	Team (and Training)
3	Testing
4	Tranexamic acid
5	Temperature
6	Transfusion
7	Termination

Summary

- Activated promptly - every 1 minute delay associated with 5% increase in mortality
- Right patient – not all bleeding patients need an MHP activation, especially GI bleeds
- Activated through standardized communication process with clear terminology
- Team promptly assembled, team has been drilled, and a team lead is designated
- First RBC spiked within 15 minutes
- Tranexamic acid given within 60 minutes (excluding GI bleeds) – 2 gm total dose for adults
- Blood work at activation and every 60 minutes or every 4 units of RBC
- Transfusion to target values and keep hemoglobin 80-120 g/L throughout
- Start with a 2:1 ratio of red cells to plasma
- Avoid hypothermia
- Terminate when hemorrhage is controlled, hemodynamics are improving, coagulation tests going in right direction, and rate of transfusion has slowed
- Don’t waste blood – we are the stewards of the blood system

Callum JL, et al. CMAJ Open. 2019 Sep 3;7(3):E546-E561