Massive Hemorrhage Protocol

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

Jeannie Callum, BA, MD, FRCPC

Director of Transfusion Medicine, Kingston Health Sciences Centre

Professor, Queen's University, Kingston, Canada

Professor, University of Toronto, Canada

Disclosures

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Outline

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

Case

- 15 year old female struck by pick-up truck while crossing the street at high speed
- Transported by helicopter to the trauma centre – injury to arrival time is 34 minutes
- Patient receives 500 mL crystalloid and 1 unit of male donor O-neg K-neg low-titre whole blood in the helicopter
- 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 trauma patient and 4 units of unmatched O-negative, K-negative red cells requested in a cooler

Case

- On arrival: obtunded, GCS 12, intubated immediately, HR 125bpm, sBP 70 mmHg, temp 35.5°C
- Massive hemorrhage protocol activated
  - Right mechanism of injury for major hemorrhage PLUS Shock Index >1.4
- Two RBC units started via rapid infuser blood warmer
- TXA 2 gram bolus given after verifying not administered in the helicopter
- Two large bore catheters inserted and surgery resident inserting 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, and viscoelastic testing
- 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 RL and 2u 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 dose 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

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 **different at every hospital**
- 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 minimum 2:1 ratio until results available
- Ratio-based resuscitation only until lab results arrive (about 60 minutes)
- Avoid hypothermia
- Terminate when patient meets termination criteria
- Don’t waste blood

Callum J, et al. CMAJ Open. 2019 Sep 3;7(3):E546-E561
Petrosoniak A, et al. Emerg Med Clin North Am. 2023 Feb;41(1):51-69
Callum J, et al. CMAJ. 2023 Jun 5;195(22):E773-E781

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

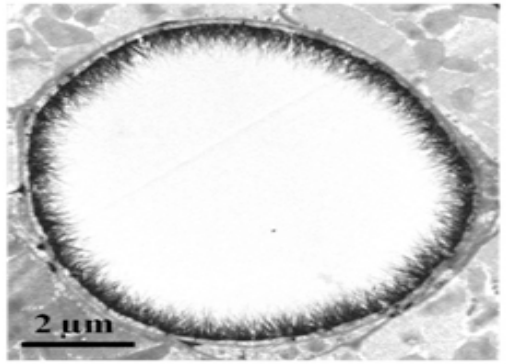
- Massive Hemorrhage Protocol (MHP) = a protocolized response to a massively bleeding patient (not all patients will end up receiving a massive transfusion)

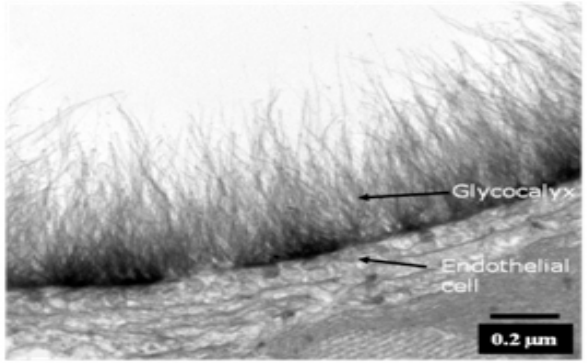
The fight for the right name

- Massive **transfusion** protocol (MTP)
- **Massive hemorrhage** protocol (MHP)
- **Major** hemorrhage protocol (MHP)

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

Pre-hospital?

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

SWIFT

SWIFT
Study of Whole blood
In Frontline Trauma

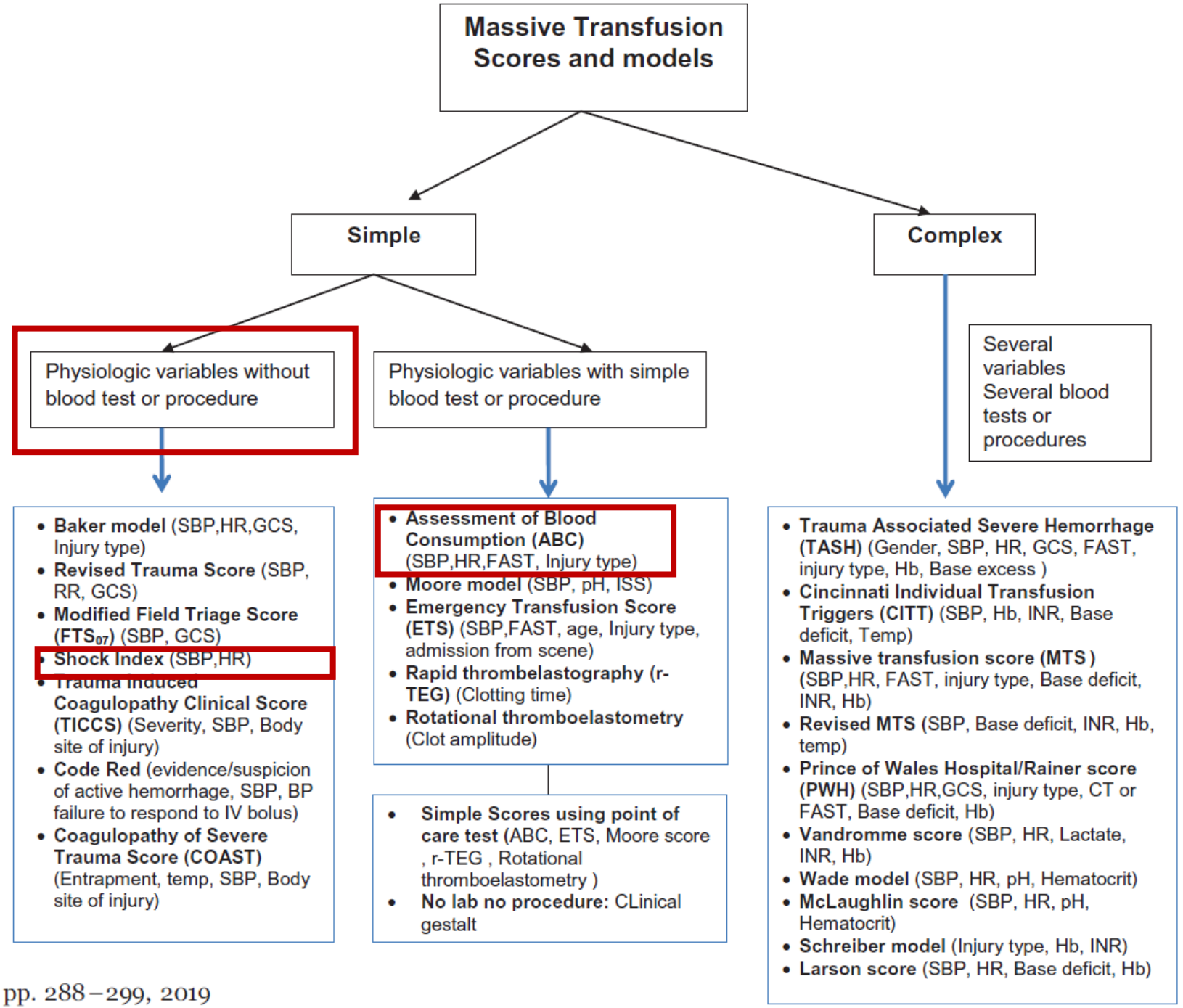
Study Design	Multi-centre, interventional, randomized, unblinded, parallel controlled trial Participants will be randomized 1:1 to intervention and comparator
Trial Participants	Patients (adults) attended by Ornge Air Ambulance Service, who have suffered major traumatic hemorrhage pre-hospital
Setting	Prehospital Emergency Medicine
Interventions to be compared	Intervention arm: Up to **two units of whole blood (WB)** Comparator arm: Up to **two units of red blood cells (RBCs) and two units of plasma**

2 Right kind of patient

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

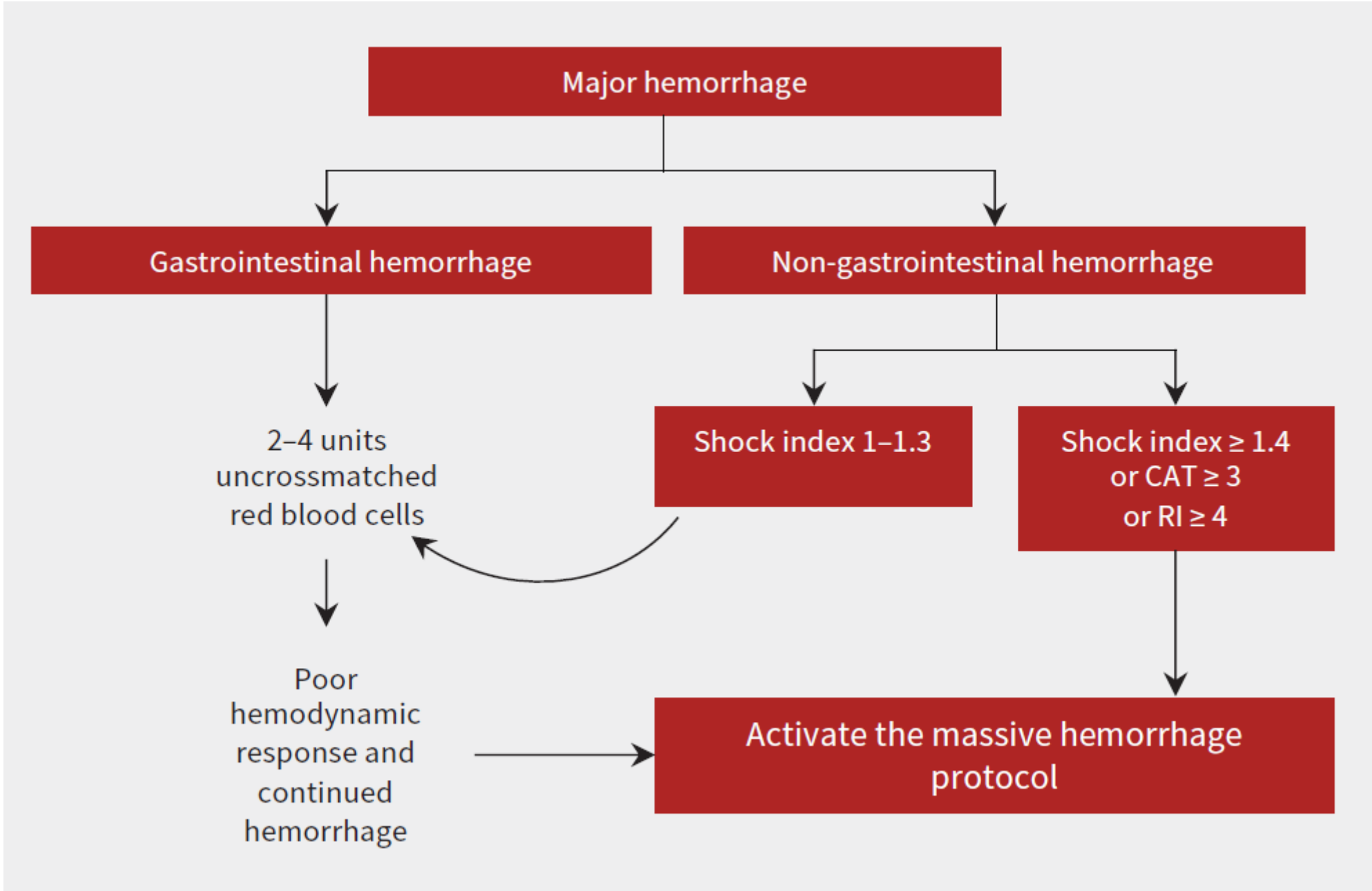
Bad hemodynamics ⇨
High heart rate
Low systolic blood pressure
Needing inotropes
Cardiac arrest
Poor response to fluids

It would be better not to need lab tests

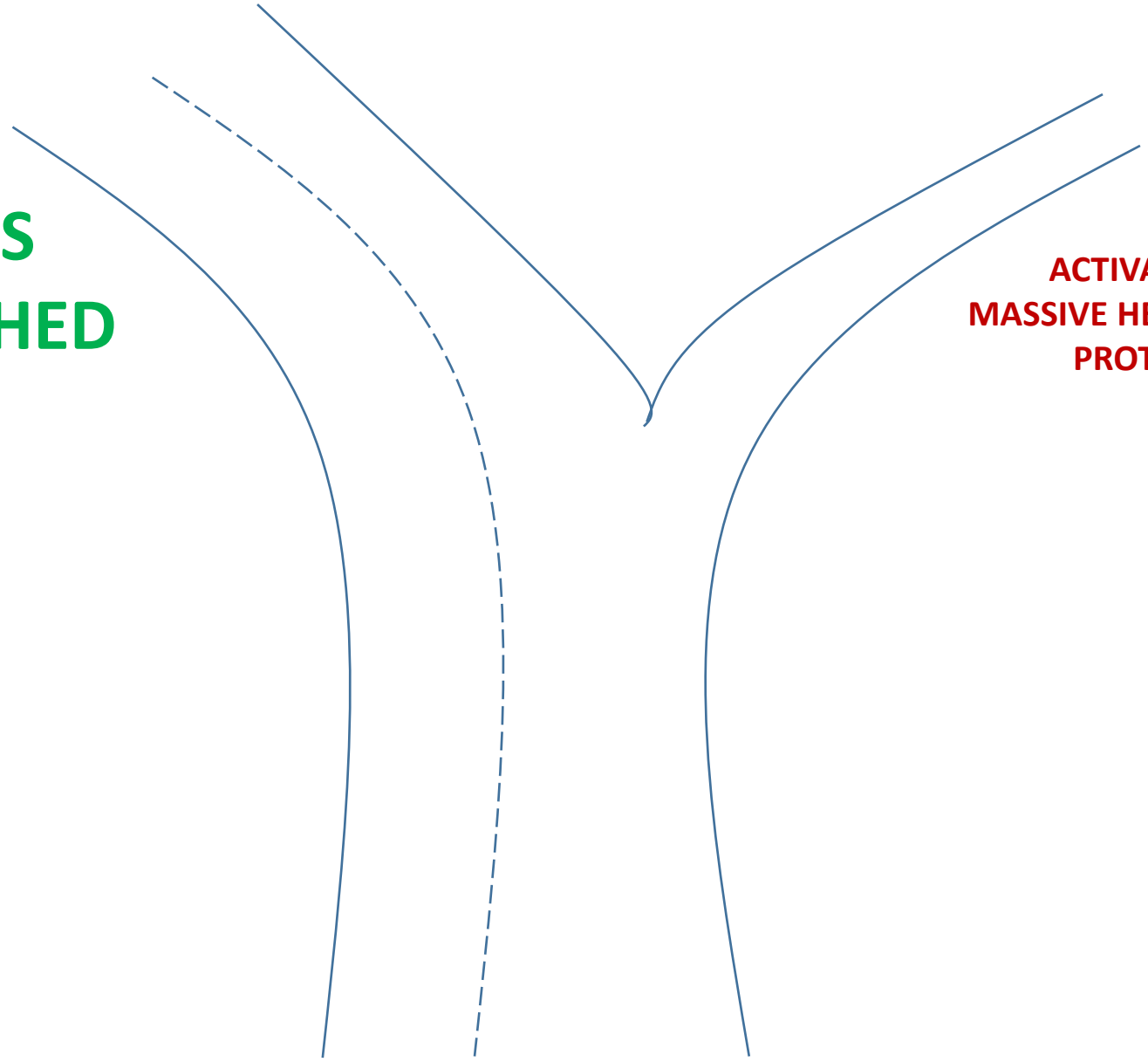


Clinician gestalt is no better either!

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


Major hemorrhage
Gastrointestinal hemorrhage
Non-gastrointestinal hemorrhage
2–4 units uncrossmatched red blood cells
Shock index 1–1.3
Shock index ≥ 1.4 or CAT ≥ 3 or RI ≥ 4
Poor hemodynamic response and continued hemorrhage
Activate the massive hemorrhage protocol

4 UNITS UNMATCHED



ACTIVATE THE MASSIVE HEMORRHAGE PROTOCOL

Bleeding patient

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)

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

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

Cirrhosis Portal HTN Guidelines (Baveno VII)

6.36 In the AVB episode, transfusion of fresh frozen plasma is not recommended as it will not correct coagulopathy and may lead to volume overload and worsening of portal hypertension. (**B.1**) (**New**)

6.37 In the setting of AVB, there is no evidence that platelet count and fibrinogen levels are correlated with the risk of failure to control bleeding or rebleeding. However, in case of failure to control bleeding, the decision to correct the haemostatic abnormalities should be considered on a case-by-case basis. (**D.2**) (**New**)

de Franchis R, et al. J Hepatol. 2022 Apr;76(4):959-974

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

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

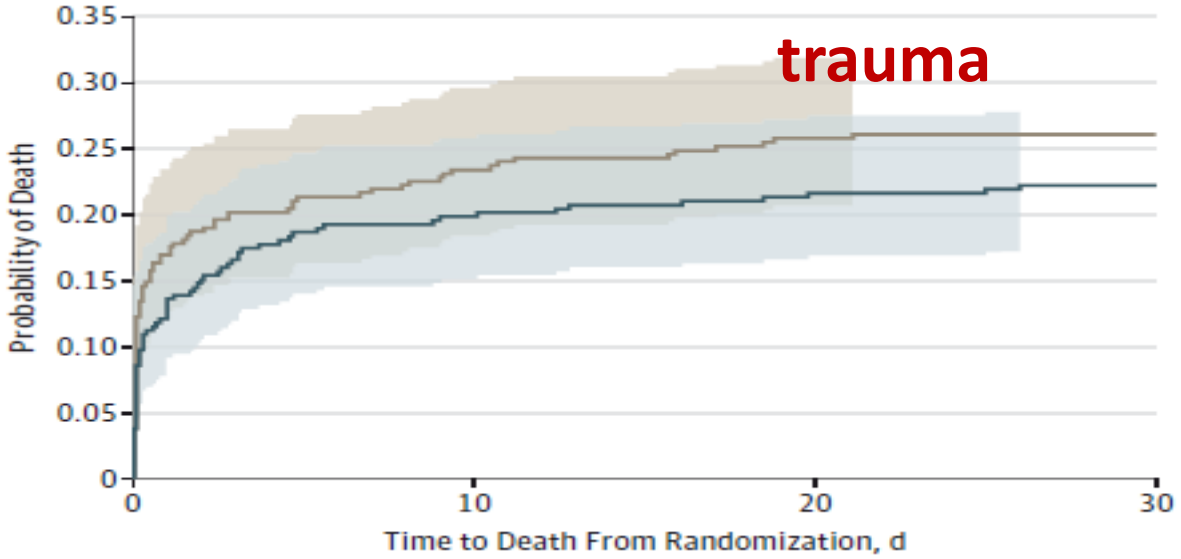
e.g.

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 (e.g. more platelets, PCC, or fibrinogen)
- Pediatric weight based coolers for kids

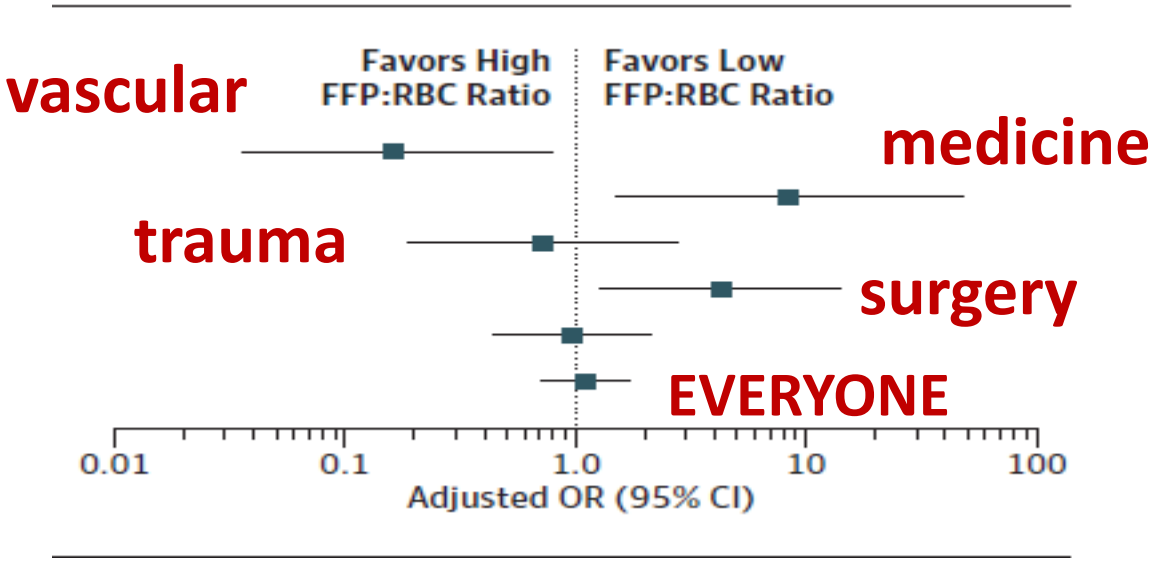
1:1 = 2:1

PROPRR



Holcomb, JAMA 2015; 313: 471-482

JAMA SURG HARVARD



Mesar, JAMA Surg 2017; March 8.

Table 2. Trial Outcomes by Treatment Group

	1:1:1 Group (n = 338)	1:1:2 Group (n = 342)	Difference (95% CI), %	Adjusted RR (95% CI)	*P* Value[a]
24-h Mortality, No. (%)[b]	43 (12.7)	58 (17.0)	−4.2 (−9.6 to 1.1)	0.75 (0.52 to 1.08)	.12
30-d Mortality, No. (%)[b]	75 (22.4)	89 (26.1)	−3.7 (−10.2 to 2.7)	0.86 (0.65 to 1.12)	.26
Achieved hemostasis					
No. (%)	291 (86.1)	267 (78.1)			.006
Anatomic, median (IQR), min[c]	105 (64 to 179)	100 (56 to 181)			.44
Hospital-free days, median (IQR)[c,d]	1 (0 to 17)	0 (0 to 16)			.83
Ventilator-free days[d]					
Total No. of patients	337	340			
Median (IQR)[c]	8 (0 to 16)	7 (0 to 14)			.14
ICU-free days[d]					
Total No. of patients	337	340			
Median (IQR)[c]	5 (0 to 11)	4 (0 to 10)			.10
Incidence of primary surgical procedure	290 (85.8)	284 (83.0)	2.8 (−2.8 to 8.3)		
Disposition at 30 d, No. (%)[e]					
Home	118 (34.9)	105 (30.7)			
Remained hospitalized	82 (24.3)	77 (22.5)			
Other[f]	59 (17.5)	71 (20.8)			.37
Morgue	75 (22.2)	89 (26.0)			
Unknown	4 (1.2)	0			
Glasgow Outcome Scale-Extended score					
Total No. of patients[g]	30	28			
Median (IQR)[c]	4 (3 to 6)	4.5 (3.5 to 7.0)			.11

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

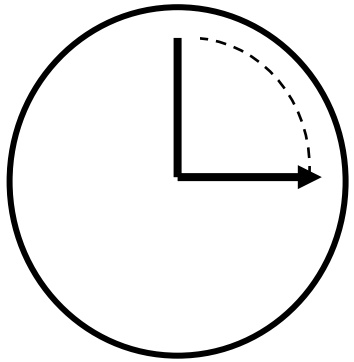
Recommendation 25 In the initial management of patients with expected massive haemorrhage, we recommend one of the two following strategies:

- 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

4 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

Callum J, Evans CCD, Barkun A, Karkouti K. CMAJ. 2023 Jun 5;195(22):E773-E781

Table 1: Key randomized controlled trials to inform the clinical management of patients with a major hemorrhage

Trial	No. of patients	Findings
Tranexamic acid		
CRASH-2[4]	20 211	Tranexamic acid reduced all-cause mortality in bleeding trauma patients.
WOMAN[5]	20 060	Tranexamic acid reduced death from bleeding in women with postpartum hemorrhage.
HALT-IT[6]	12 009	Tranexamic acid did not reduce the risk of death from bleeding in patients with gastrointestinal hemorrhage and was associated with higher rates of thromboembolic complications.
ATACAS[7]	4662	Tranexamic acid reduced the risk of transfusion and need for re-operation for bleeding in patients undergoing cardiac surgery.
POISE-3[8]	9535	Tranexamic acid decreased the risk of major bleeding after noncardiac surgery.
STAAMP[9]	927	Tranexamic acid did not decrease mortality at 30 d for all bleeding trauma patients. Mortality was lower in the subgroup of patients administered tranexamic acid within 1 h and with severe shock (systolic pressure < 70 mm Hg).

Systematic review (Mortality, Trauma)

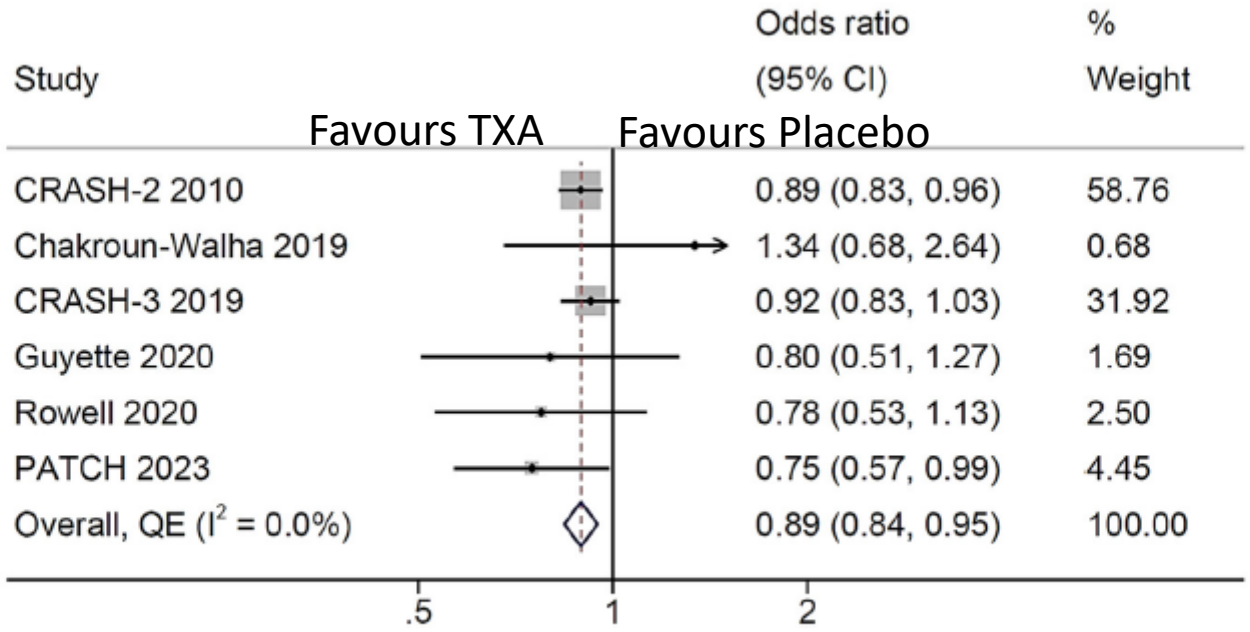


Figure 2. Forest plot depicting estimated effects of each trial and the meta-analytic effect. Odd ratios indicate the odds of mortality with tranexamic acid compared to placebo at one month. *CI*, confidence interval.

Fouche PF, et al. Ann Emerg Med. 2023 Nov 22:S0196-0644(23)01

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.

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.

ROC-TXA infusion rate

5.2.7 Justification for dose selection

The dose selection for the study drug is as follows:

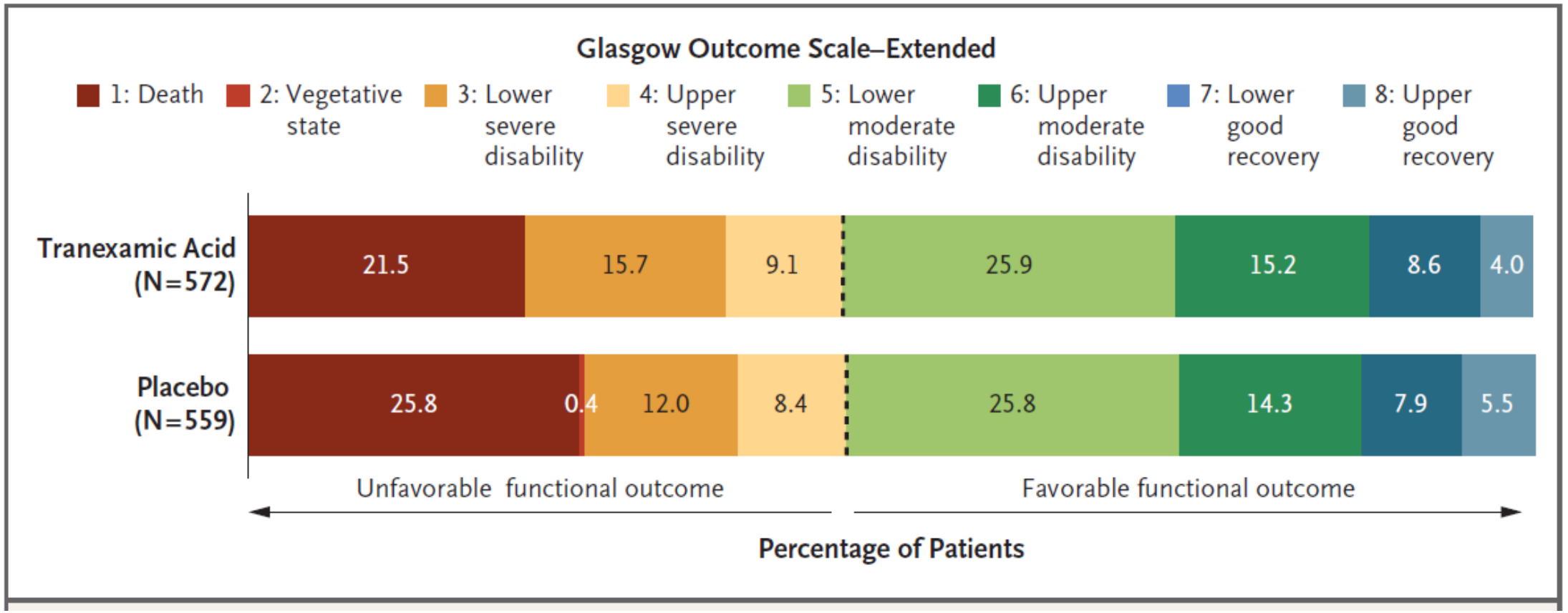
- *Bolus/maintenance arm*: 1 gram IV TXA in 250 mL administered wide open followed by a 1 gram maintenance IV TXA infusion over 8 hours (weight based equivalent: 50 kg person – bolus 20 mg/kg, maintenance 2.5 mg/kg/h; 75 kg person – bolus 13.3 mg/kg, maintenance 1.7 mg/kg/h; 100 kg person – bolus 10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

Tranexamic acid

Patient type	Dose
Trauma	2 grams iv within 1 hour of injury
Postpartum hemorrhage	1 gram iv within 1 hour of onset of bleed 1 gram iv at 30 min if bleeding continues
Cardiac surgery	TXA pre-sternotomy (low and high dose options)
Non-cardiac major surgery	1 gram iv at start 1 gram iv at end
Gastrointestinal bleeding	No

Controversy – PATCH-Trauma



Shakur-Still H, Roberts I. N Engl J Med. 2023 Jul 13;389(2):181-183 (editorial)

PATCH-Trauma Investigators and the ANZICS Clinical Trials Group. Prehospital Tranexamic Acid for Severe Trauma. N Engl J Med. 2023 Jul 13;389(2):127-136

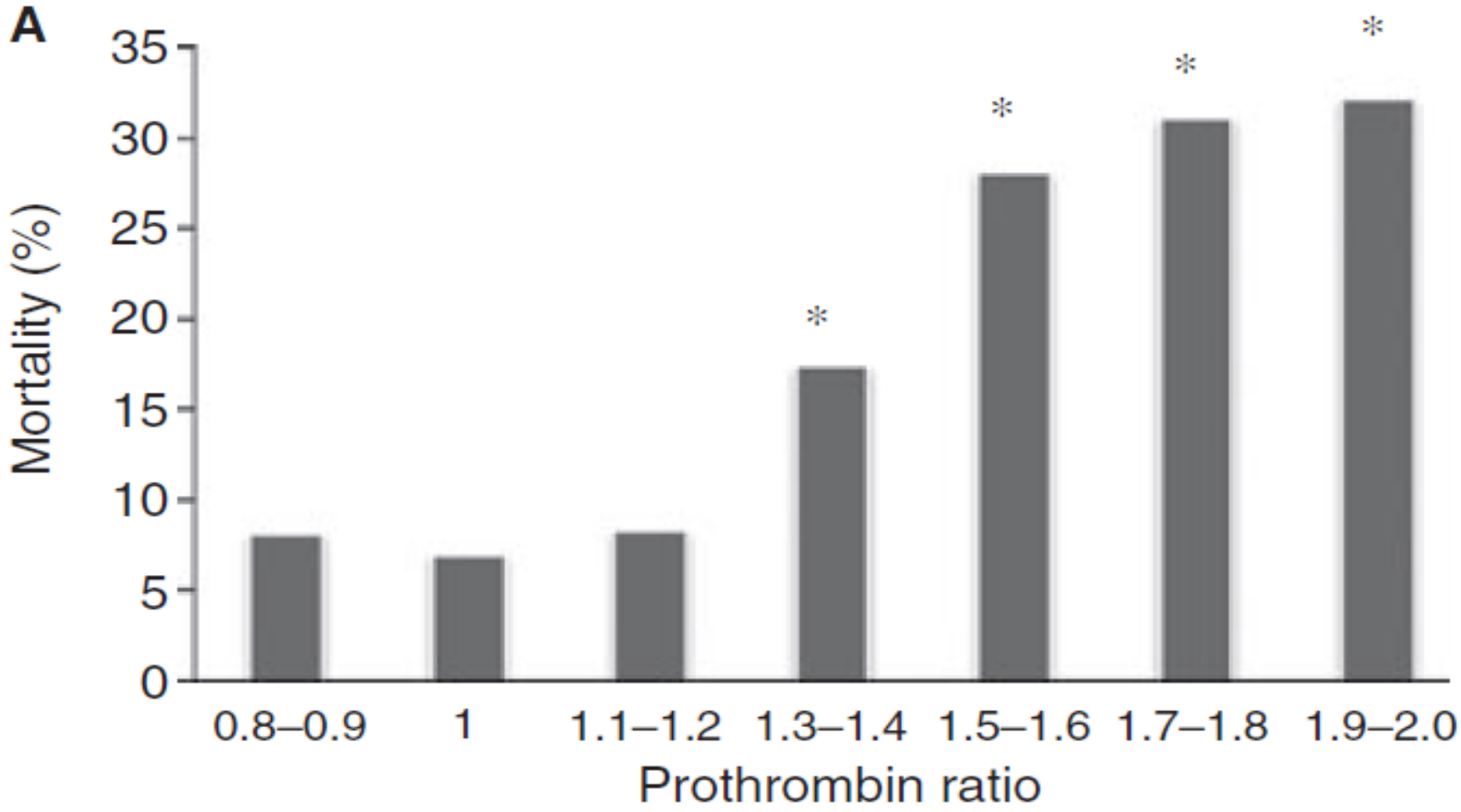
5 Blood work at activation and hourly

- 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

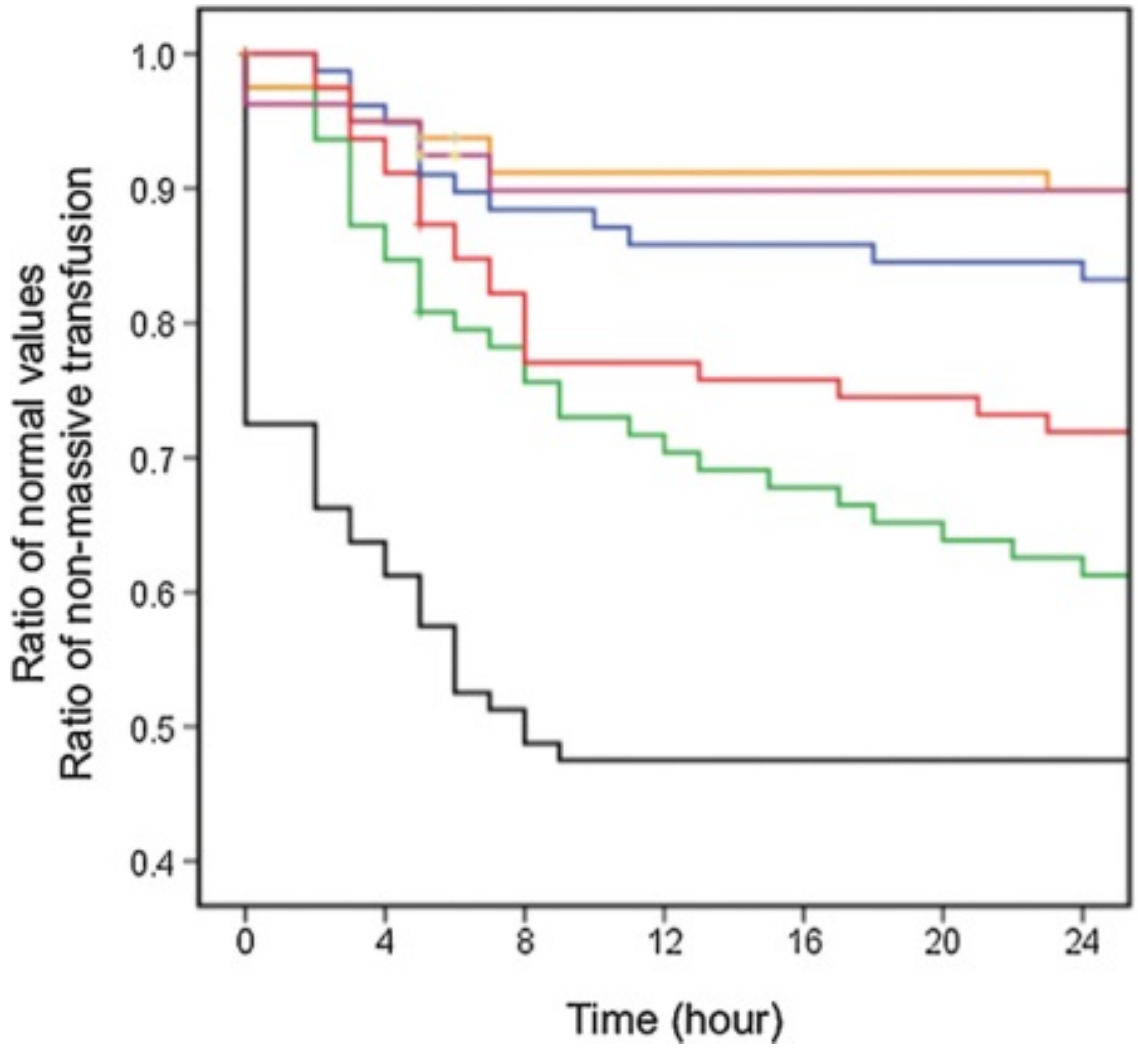
Mortality increases at >1.2

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



PT-INR ≥ 1.5
APTT ≥ 60sec
Platelet counts
≤ 50 x10⁹/L

<20% patients

Massive transfusion

Platelet counts
≤ 100 x10⁹/L

Fibrinogen
≤ 1.5 g/L

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

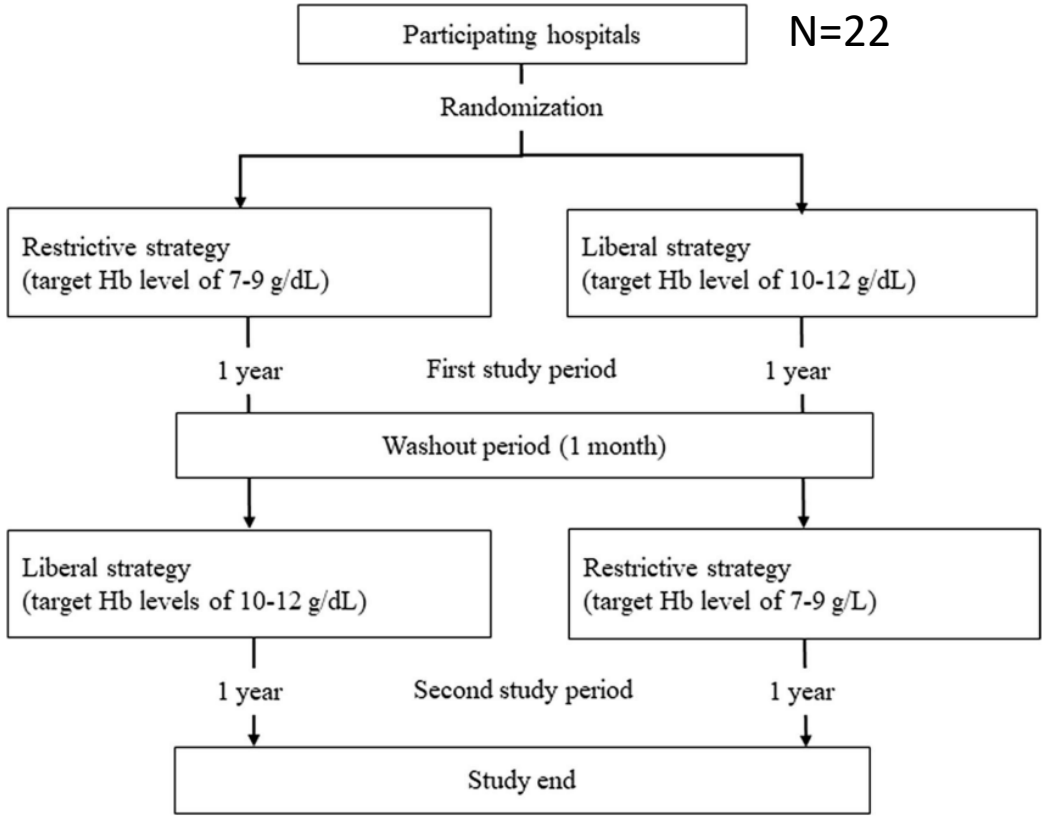
Baksaas-Aasen K, Gall LS, Intensive Care Med. 2021 Jan;47(1):49-59.

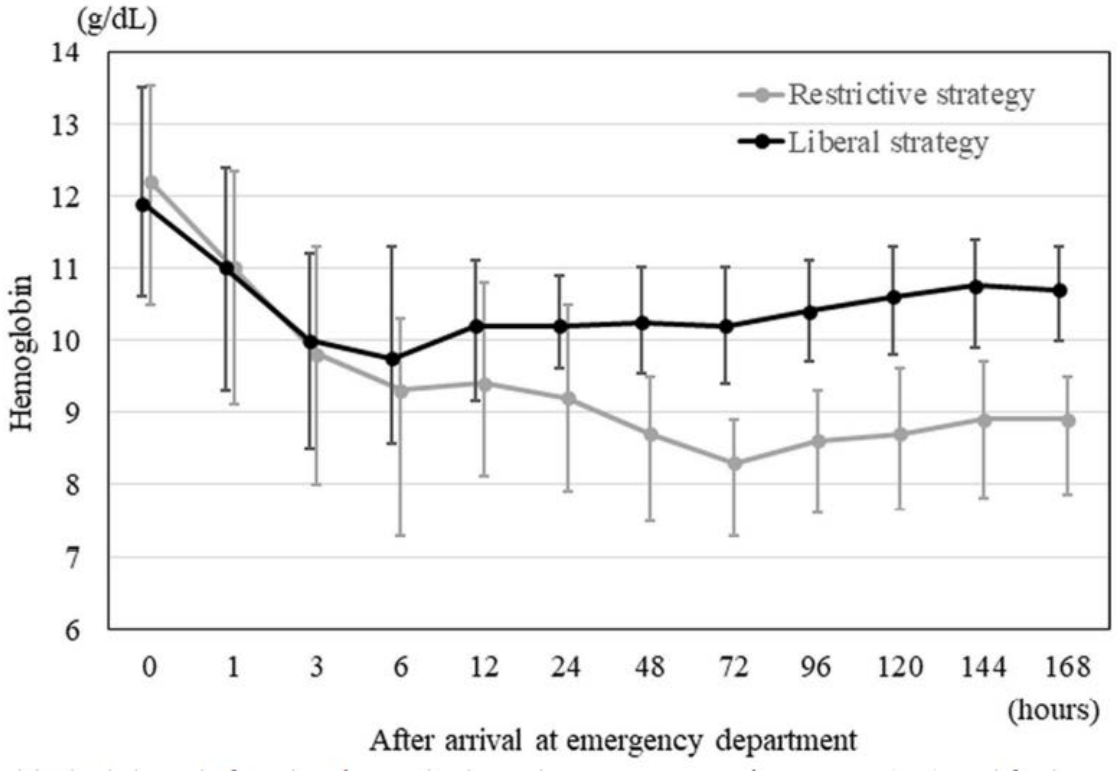
6 Transfuse to Target

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	70-90 g/L
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)

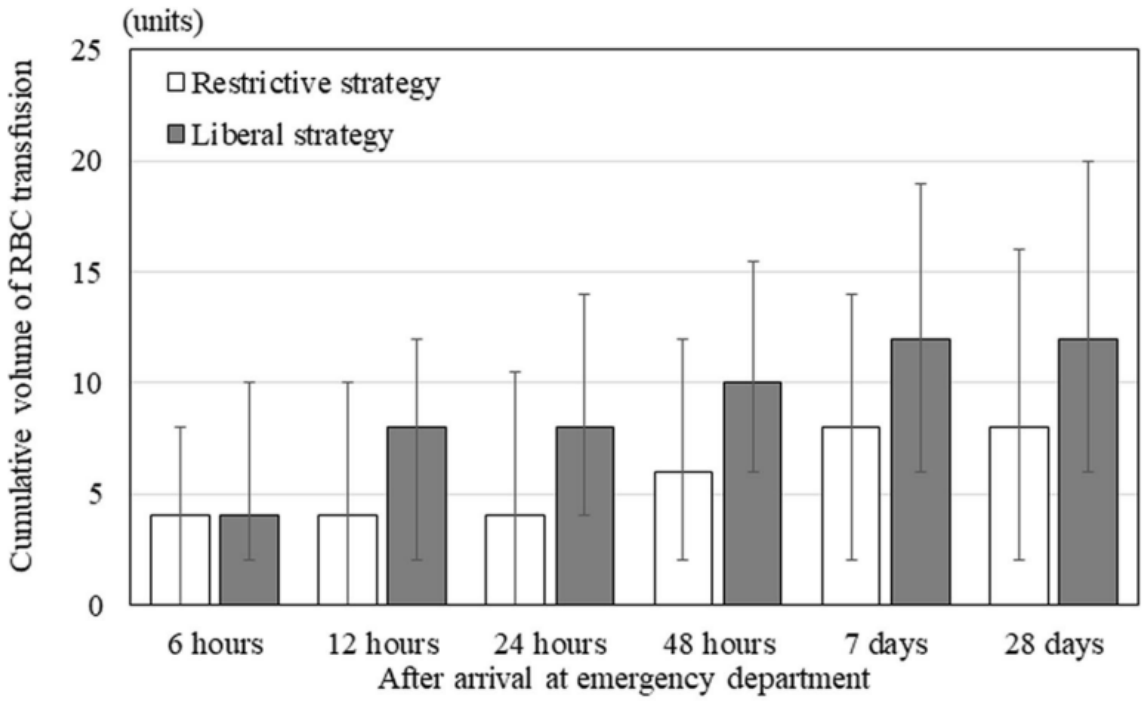
RESTRIC Trial – ED trial in severe trauma, n=411



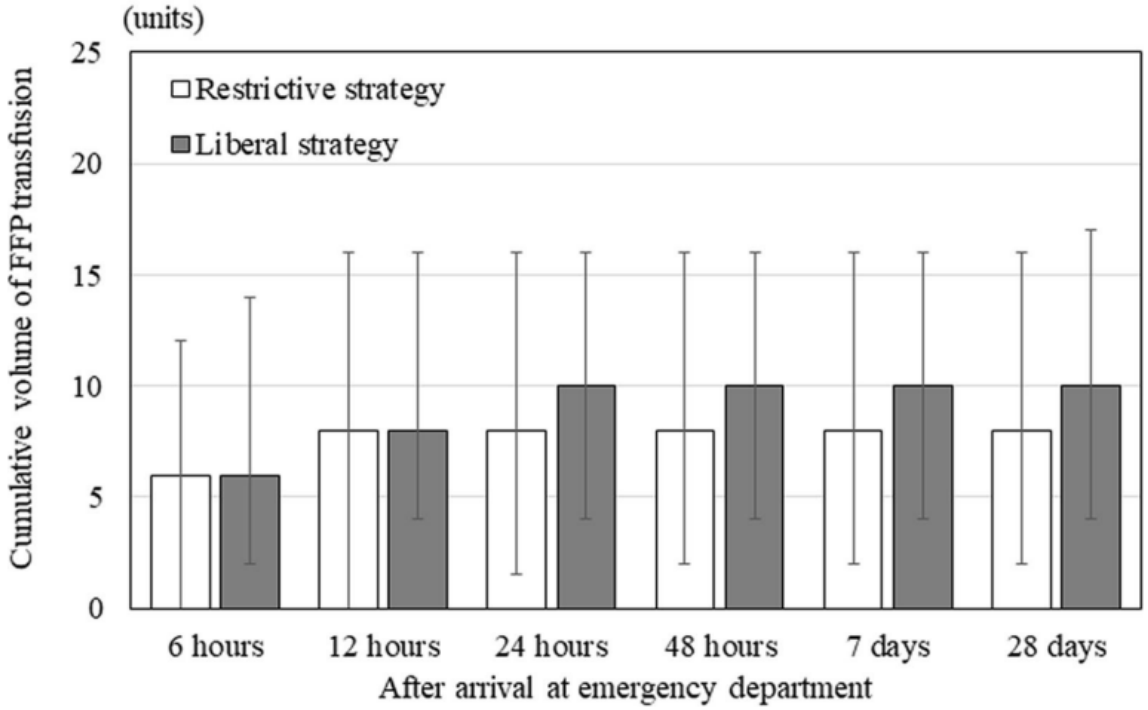


Hayakawa *et al. Journal of Intensive Care* (2023) 11:34
https://doi.org/10.1186/s40560-023-00682-3

RESTRIC Trial



Red Blood Cells

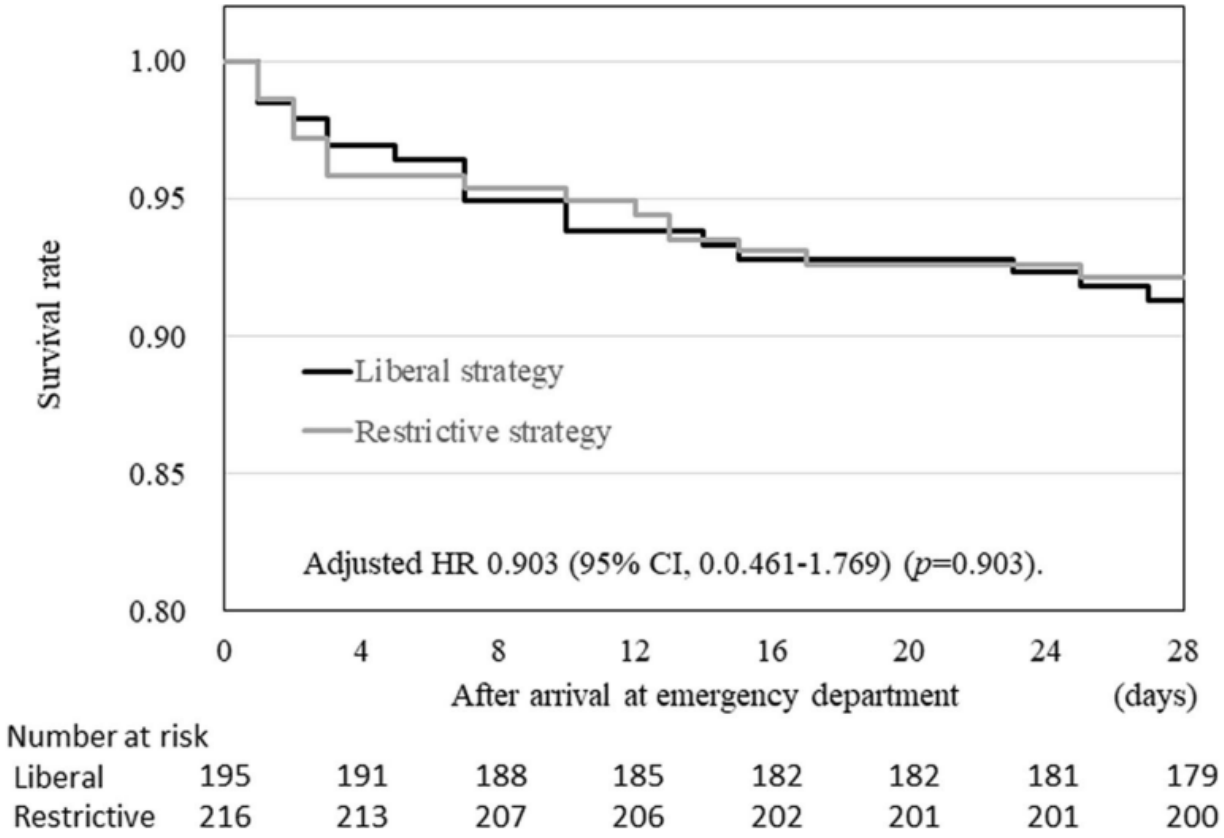


Plasma

RESTRIC Trial

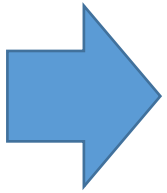
No difference in any other Outcomes

No differences found in the subgroup analyzes



ORACL Trial

- Patients: Ortho trauma past initial resuscitation phase, hemodynamically stable, aged 18-50, Hb<90 g/L
- N=65
- Multicentre trial
- Intervention: Restrictive threshold 55 g/L
- Control: Liberal threshold 70 g/L
- Time: 1 year follow-up
- Outcome: Infection



Lower transfusion rate after randomization – 46 vs. 94%

Lower infection rate – 6 vs. 25%, p=0.012

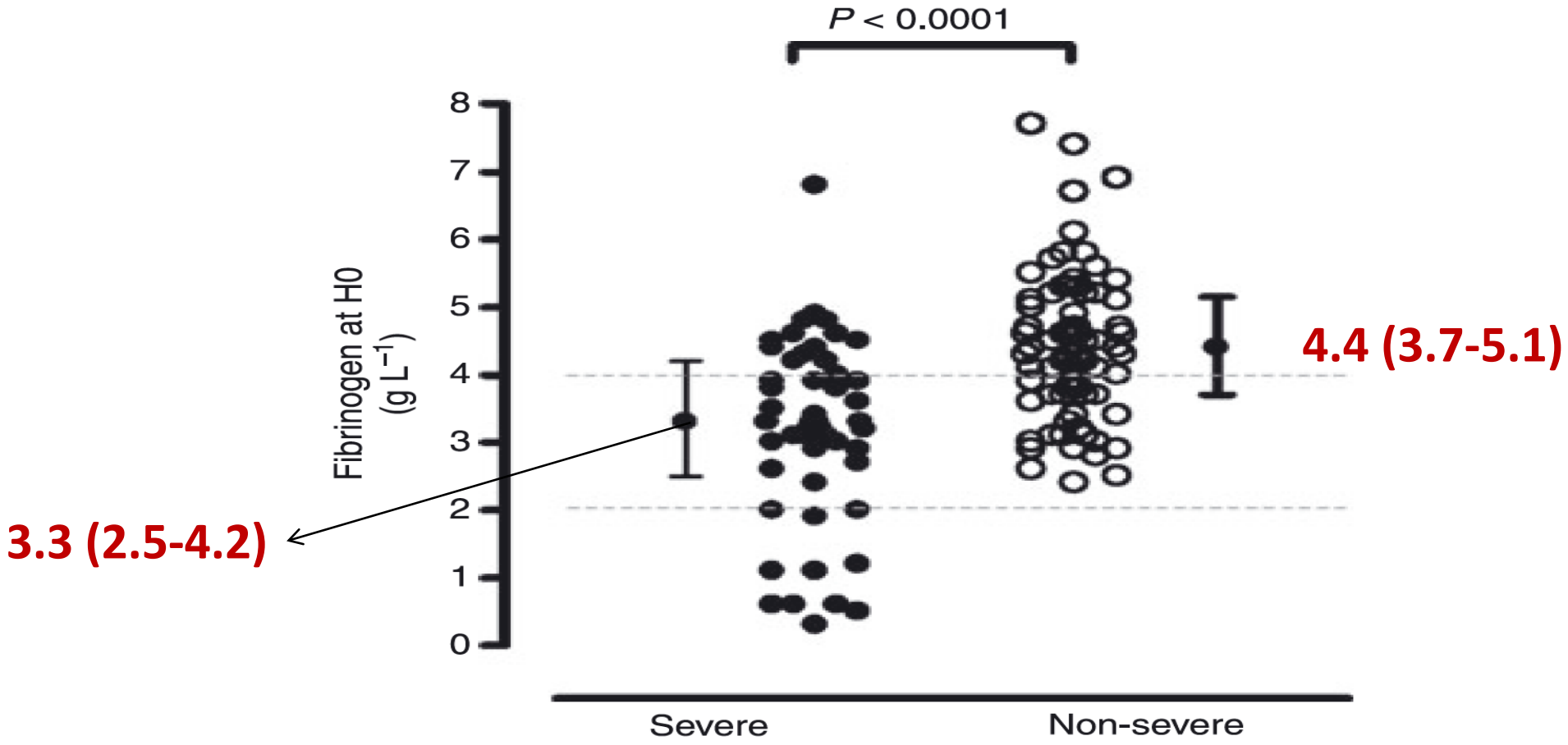
Longer length of stay – 11.5 vs. 9 days, p=0.04

No differences in any other outcome

Mullis BH, et al. J Orthop Trauma. 2024 Jan 1;38(1):18-24

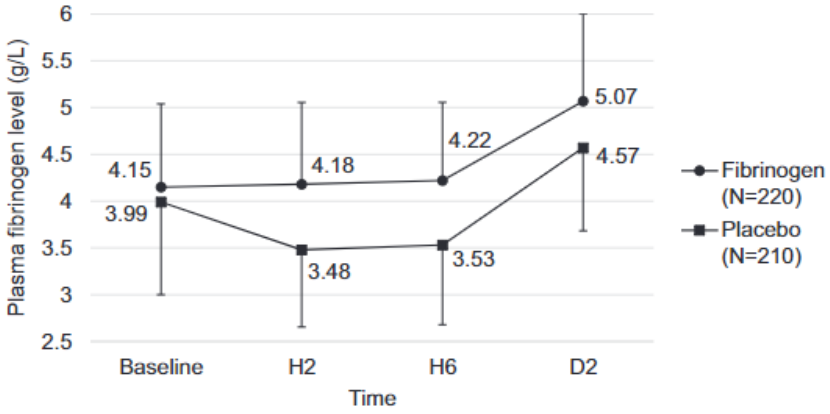
Fibrinogen<2.0 g/L and PPH

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



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

PPH - No pre-emptive Fibrinogen – FIDEL Trial



50% got TXA
80% atony
<1% had fibrinogen <2 g/L

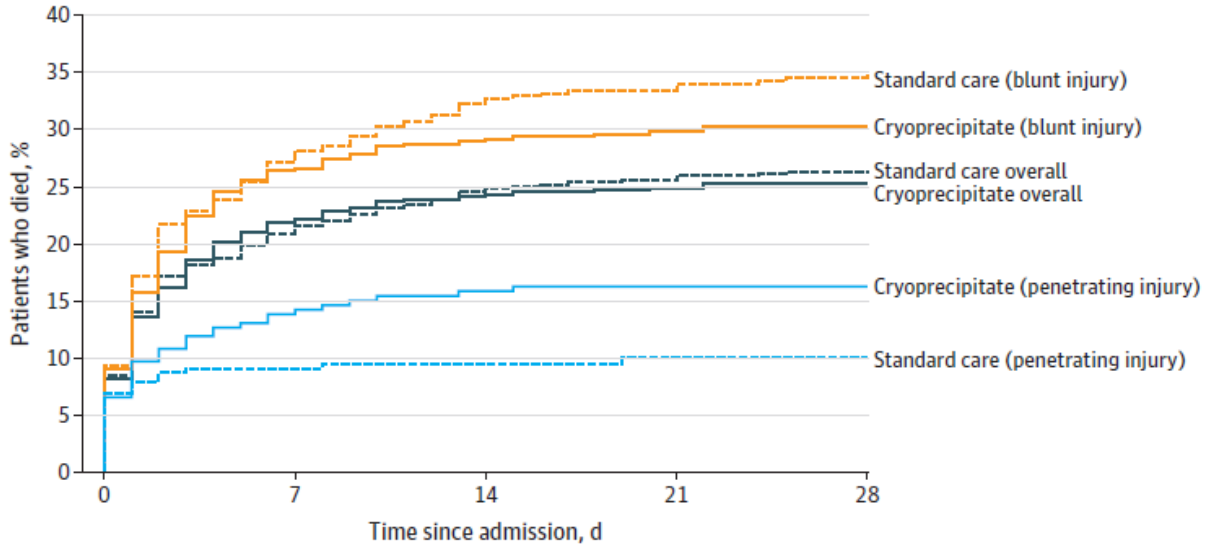
Table 2. Primary and secondary outcomes — 3 grams

Outcome	Fibrinogen *n* = 220	Placebo *n* = 210	OR (95%CI)	*P*-value
Primary outcome				
Failure, *n* (%)	88 (40.0%)	89 (42.4%)	0.99 (0.66–1.47)	0.96*
Secondary outcomes				
RBC transfusion ≥2 Units from H0 to D2, *n* (%)	51 (23.4%)	52 (25.0%)	1.00 (0.63–1.60)	0.98*
RBC transfusion ≥4 Units from H0 to D2, *n* (%)	6 (2.7%)	5 (2.4%)		0.87**
Number of RBC units per transfused patient from H0 to D2, mean ± SD	2.7 ± 1.2	3.1 ± 2.5		0.99***
Hb loss ≥4 g/dl from reference level to D2, *n* (%)	42 (19.1%)	41 (19.5%)	1.02 (0.62;1.67)	0.95*
Hb loss ≥3 g/dl from reference level to D2, *n* (%)	102 (46.4%)	98 (46.9%)		0.91**
Hb loss ≥4 g/dl from H0 to D2, *n* (%)	16 (7.3%)	17 (8.3%)		0.69**
Hb level < 9 g/dl from reference level to D2, *n* (%)	112 (50.9%)	117 (56.0%)		0.29**
Total blood loss (from baseline to D2), mean ± SD, ml	1555 ± 849	1723 ± 1193		0.21***
Additional blood loss (from H0 to D2), mean ± SD, ml	304.7 ± 386.2	319.7 ± 417.1		0.33***
Intrauterine balloon, *n* (%)	63 (28.6%)	61 (29.0%)		0.93**
At least one rescue procedure, *n* (%)	65 (29.5%)	64 (30.5%)		0.83**
At least one invasive haemostatic procedure, *n* (%), including:	8 (3.6%)	10 (4.8%)		0.56**
Arterial embolisation	6 (2.7%)	10 (4.8%)		0.27**
Arterial ligation	0 (0%)	0 (0%)		—
Hysterectomy	0 (0%)	1 (0.5%)		0.49****
Intensive care or resuscitation, *n* (%)	62 (28.2%)	54 (25.7%)		0.56**
Length of stay in intensive care or resuscitation unit, mean ± SD, day	0.7 ± 0.6	0.7 ± 0.9		0.84***
SOFA score of patients admitted to intensive care or resuscitation unit, median [min; max]	0 [0;4]	0 [0;6]		0.32***
Death, *n* (%)	0 (0%)	0 (0%)		—

Ducloy-Bouthors AS, et al. BJOG. 2021;128:1814-1823

Trauma – No pre-emptive fibrinogen (CRYOSTAT2)

Figure 2. Mortality Overall and by Injury Type



No. of patients at risk

Cryoprecipitate overall	784	567	532	514	498
Standard care overall	795	569	518	501	479
Cryoprecipitate (blunt injury)	495	348	332	323	310
Standard care (blunt injury)	518	353	320	307	289
Cryoprecipitate (penetrating injury)	289	219	200	191	188
Standard care (penetrating injury)	277	216	198	194	190

Davenport R, et al. JAMA. 2023 Nov 21;330(19):1882-1891.

7 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.


PUI

The science behind MHPs

- 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
- First RBC spiked within 15 minutes
- Tranexamic acid given within 60 minutes of MHP (excluding GI bleeds)
- Blood work at activation and every 60 minutes or every 4 units of RBC
- Transfusion to target values and keep hemoglobin 70-90 g/L throughout
- Start with a 2:1 ratio of red cells to plasma, everything else goal-directed
- Avoid hypothermia

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

Fun homework

- Emergency Medicine Cases Podcast:
  - Ep 152 The 7 Ts of Massive Hemorrhage Protocols - Emergency Medicine Cases
- CMAJ Podcase “Optimizing nonsurgical management of major hemorrhage”
  - Podcasts | CMAJ
- First10EM by Justin Morgenstern
  - Massive hemorrhage: a very deep dive - First10EM