Patient Blood Management

The Intraoperative Period

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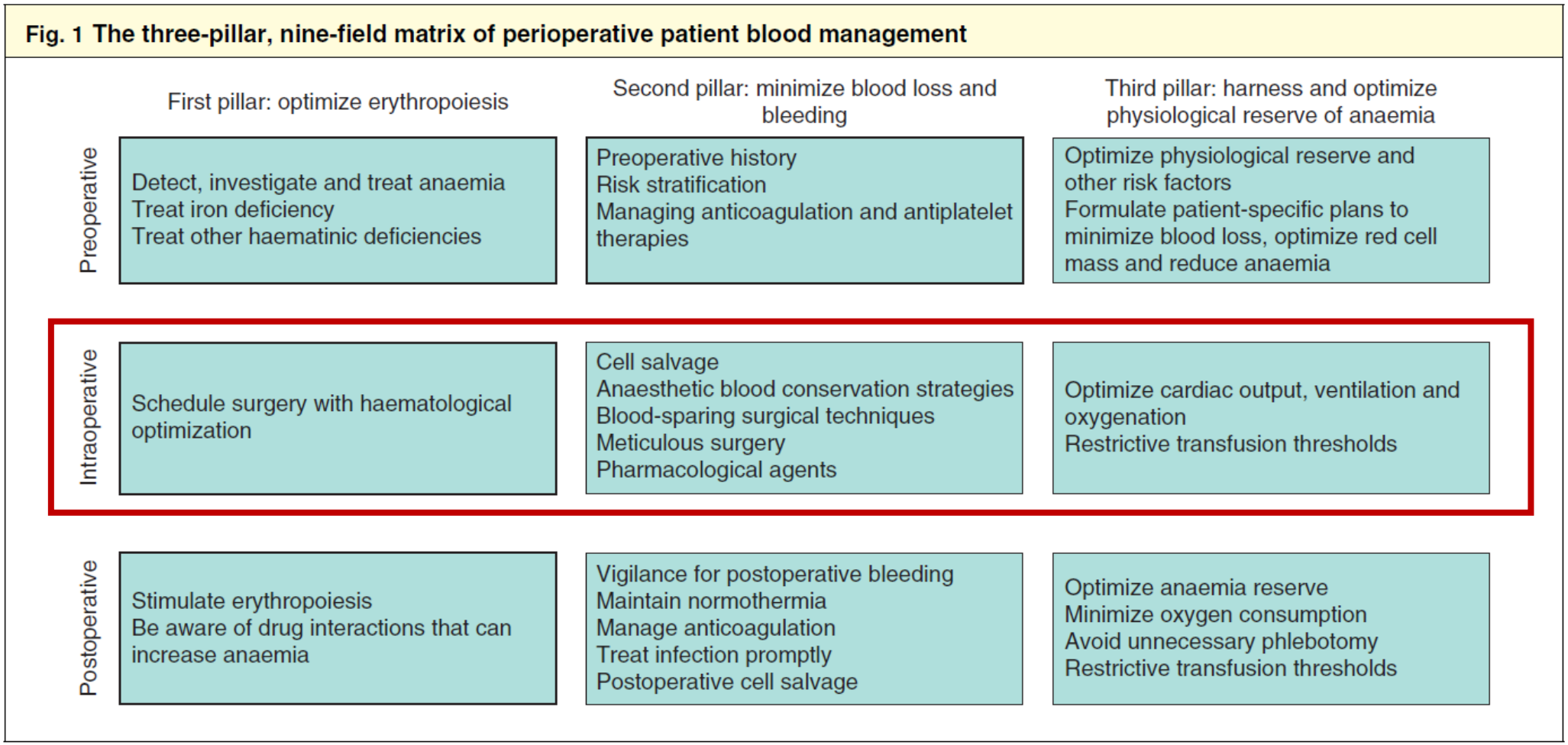
Three Pillars of PBM

Fig. 1 The three-pillar, nine-field matrix of perioperative patient blood management



Shah et al. BJS 2020;107:e26-e38

Practical Criteria for Adoption of Any Modality

1. Is it effective?

2. Is it as safe (or safer) than transfusion alternatives?

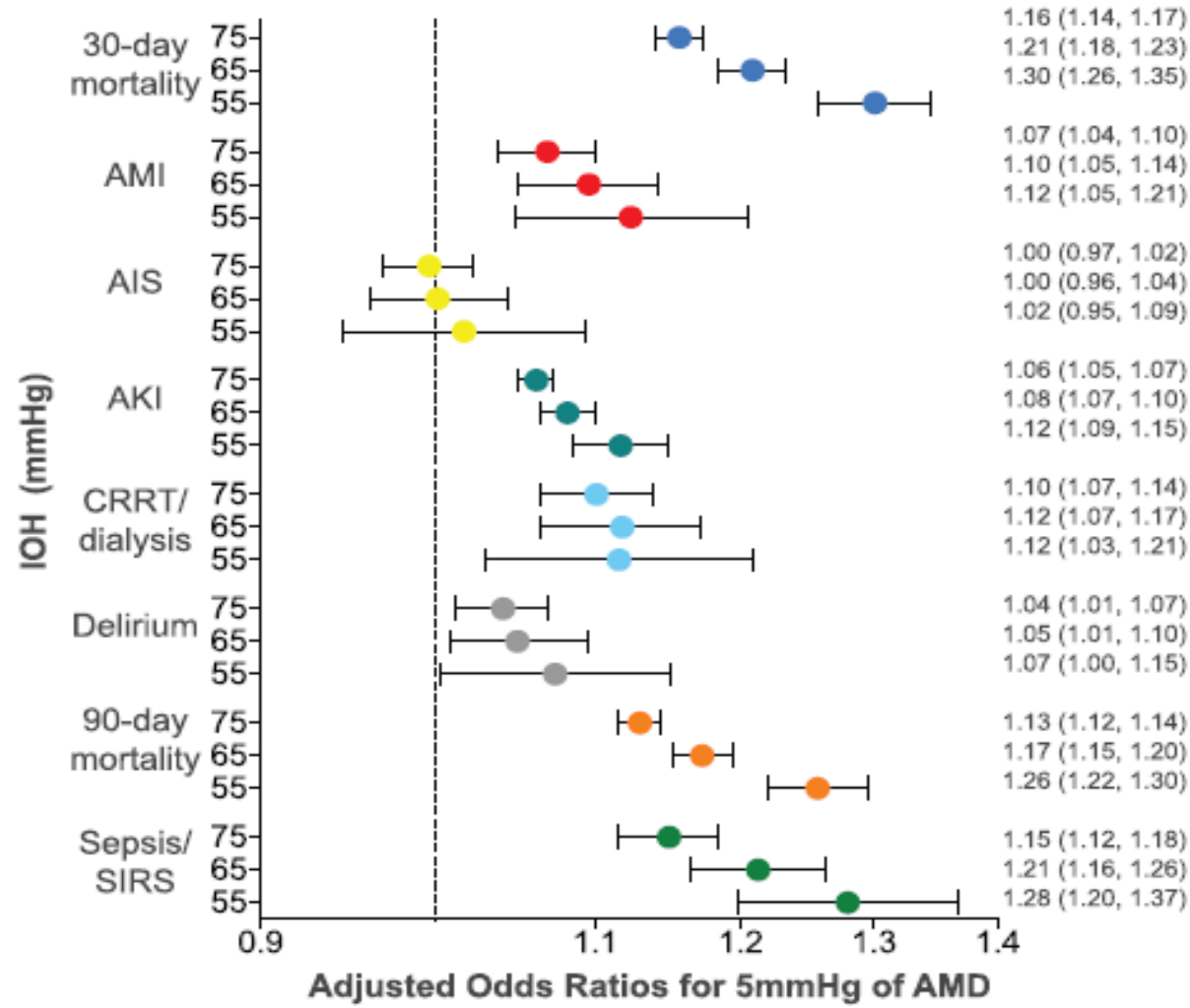
3. Are the costs reasonable?

Anesthetic blood sparing techniques

- Controlled (permissive) hypotension
  - BP maintained at mean of ~ 50–60 mmHg
  - Objectives:
    - Reducing blood loss
    - Improving visibility in surgical field
  - Multiple ways of achieving target BP:
    - Anesthetic depth, vasodilators, beta-blockers, fluid restriction
  - Supporting data is weak and primarily from small, low-quality, outdated studies
  - Safety not adequately assessed

Anesthetic blood sparing techniques

- Hypotension is associated with adverse outcomes
  - Actively maintaining a low BP therefore doesn't seem wise!



Gregory et al. Anesth Analg 2021;132:1654-1665

Neuraxial Anesthesia (Epidural/Spinal)

- Mechanism:
  - Sympathetic blockade → reduces arterial pressure
    → reduces venous pressure
    → reduces surgical stress
      → stabilizes clotting factors
      → reduces fibrinolysis

- Evidence is conflicting:
  - Older, lower quality evidence positive
  - Newer, higher quality evidence negative

Acute normovolemic hemodilution

- Removal of 3-4 units of blood before surgery and simultaneous replacement with crystalloids or colloids
  - Theoretical example:
    - if Hct = 0.40 and EBL = 1L $\rightarrow$ RBC Loss = 400 cc
    - if Hct = 0.25 and EBL = 1L $\rightarrow$ RBC Loss = 250 cc
    - RBC conserved = 150 cc or $\sim$ 2/3 of a unit of PRBC
- Supporting data is weak and primarily from small, low-quality, outdated studies
- Safety not adequately assessed

Do Anesthetic Blood Sparing Techniques Meet Adoption Criteria?

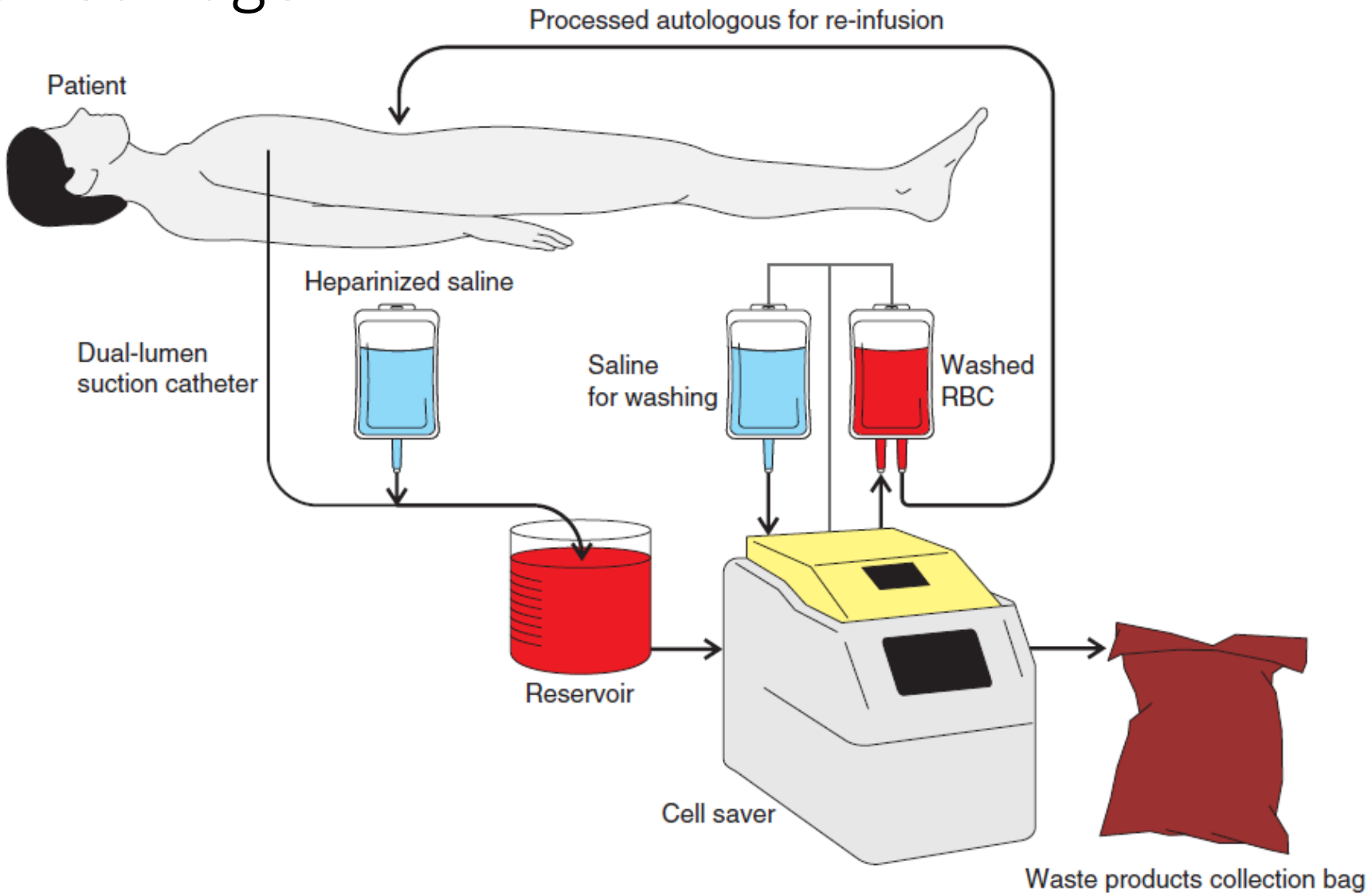
1. Is it effective? Not sure

2. Is it as safe (or safer) than transfusion alternatives? Don't know

3. Are the costs reasonable? Yes

- My recommendations:
  - Do not use for blood sparing effects
  - Use as indicated to improve visibility in field of surgery (e.g., ENT)
    - ↓ length of surgery + surgical control of bleeding = ↓ blood loss

Cell Salvage



Cell Salvage

- Proven safety with modern machines
  - Risks: Hemolysis, air embolism, incomplete washing, infections
  - Washing removes: >90% viable RBCs, >90% washout; >95% Free Hb and albumin; goal is 55-80% Hct
  - Safer than allogeneic blood
    - Lower AE rates (0.027% versus 0.14%); Better quality (fresh versus old blood)
- Indications
  - High anticipated blood loss:
    - > 500-1000 mL; 10-20% of BV; 1-2 units of recovered RBC
  - Anemia, antibodies or rare blood types, JW
- Benefits
  - Reduce RBC exposure
    - On average, ↓0.7 units; ↑avoidance ~40%; More effective when massive bleeding

Ashworth et al. BJA 2010;105:401-416; Miquel et al. Surgeries 2022;3:44-63

Cell Salvage – Other Consideration:

- Only RBCs, so can cause dilutional coagulopathy
- Bacterial contamination risk
    - Washing removes >80% of bacteria; Leukocyte depletion filter (LDF) removes >99%
    - Transfuse collected blood within 6 hours
- Limit transfusions to no more than 15 unit equivalents
    - Units contain some activated WBCs, platelets, clotting and inflammatory factors
- In Cancer surgery
    - Reinfused tumour cells do not have metastatic potential
    - Not contraindicated, but general recommendation not established
    - LDF reduces tumour load, but slows infusion rates, becomes saturated and can cause bradykinin-mediated hypotension
- PPH
    - Contamination by bacteria, amniotic fluid, fetal red cells (isoimmunization)
    - Also not cost-effective

Ashworth et al. BJA 2010;105:401-416; Miquel et al. Surgeries 2022;3:44-63

Does Cell Salvage Meet Adoption Criteria?

1. Is it effective? Yes
2. Is it as safe (or safer) than transfusion alternatives? Yes
3. Are the costs reasonable? Yes

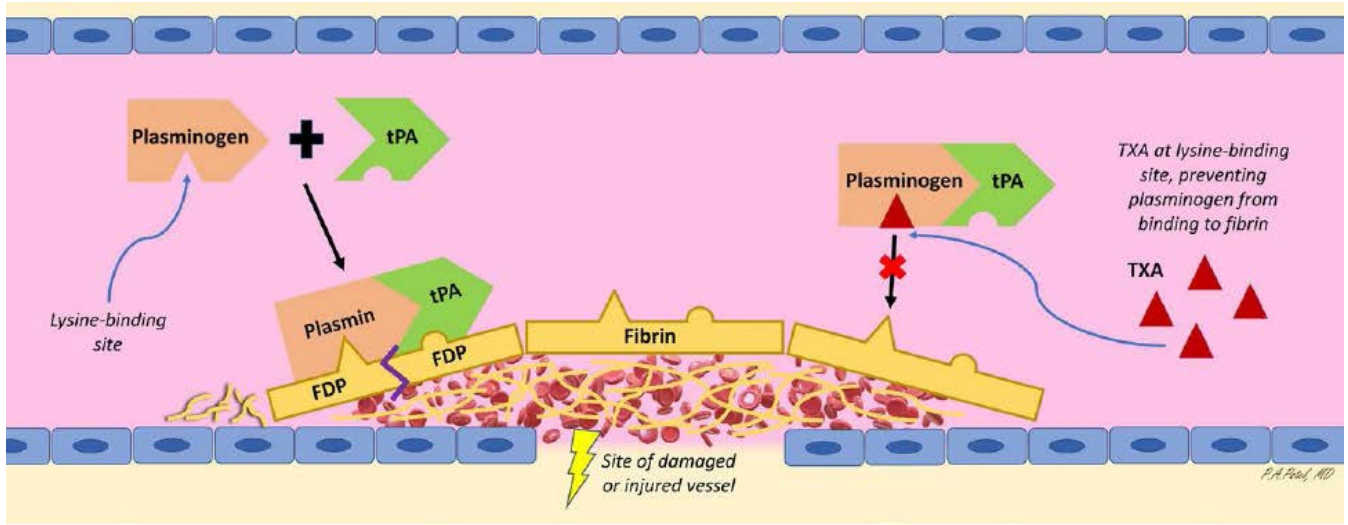
- My recommendations:
  - Use for blood sparing effects in high-blood-loss surgeries

Pharmacologic Agents

- Antifibrinolytics: Tranexamic acid
- Desmopressin (DDVP)
- Prothrombin complex concentrate (PCC); 3-factor vs. 4-factor
- Fibrinogen concentrate
- rFVIIa

Tranexamic Acid

- An old (>50 years) drug and on WHO list of essential medicines
- Almost all usage in Canada is still off-label
    - “Increased local fibrinolysis when the diagnosis is indicative of hyperfibrinolysis, as with conization of the cervix, dental extraction in patients with coagulopathies (in conjunction with antihaemophilic factor) epistaxis, hyphaema, and menorrhagia (hypermenorrhea).”
- Mechanism of action: Clot stabilizer



Patel et al. Anesth Analg 2022;135:460-73

Tranexamic Acid: General Considerations

- Hyperfibrinolysis is a contributing factor to bleeding
  - Importance varies based on patient-related and surgery-related factors
- Overall safety well established, but does have risks
  - Contraindications: Allergy, Hypercoagulable state, Seizure
  - Renally excreted and not dialyzable – dose adjustment needed
  - Seizure risk
  - Avoid in patients with recent thromboembolic events and cirrhosis?
- Dosage not fully clarified
  - Recommendations are based on specific clinical studies that did not fully consider pharmacokinetic properties of the drug

Patel et al. Anesth Analg 2022;135:460-73

Tranexamic Acid Dosage

- Pharmacokinetics:
  - Therapeutic plasma concentration is ≈10 mg/L
  - 80% inhibition requires plasma concentration of 20 mg/L
  - 100% inhibition requires plasma concentration of 100 mg/L

  - 10 mg/kg IV (≈1g) → 10 mg/L in plasma (5-6 hours)
    - Good for most situations
  - 10 mg/kg IV + 1 mg/kg/hr → 30 mg/L in plasma
    - Good for higher-risk situations
- Specific doses used:
  - CV surgery: 20-100 mg/kg (current recommendations are for the lower range)
  - Trauma: 1 gm bolus; 1 gm infusion over 8 hours

Patel et al. Anesth Analg 2022;135:460-73; McCormack Drugs 2012;72:585-617

Landmark Trauma Study

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

*CRASH-2 trial collaborators**

- N = 20,211
- Dose: 1g bolus + 1g infusion over 8 hours
- Primary outcome: 28-day in-hospital all-cause mortality

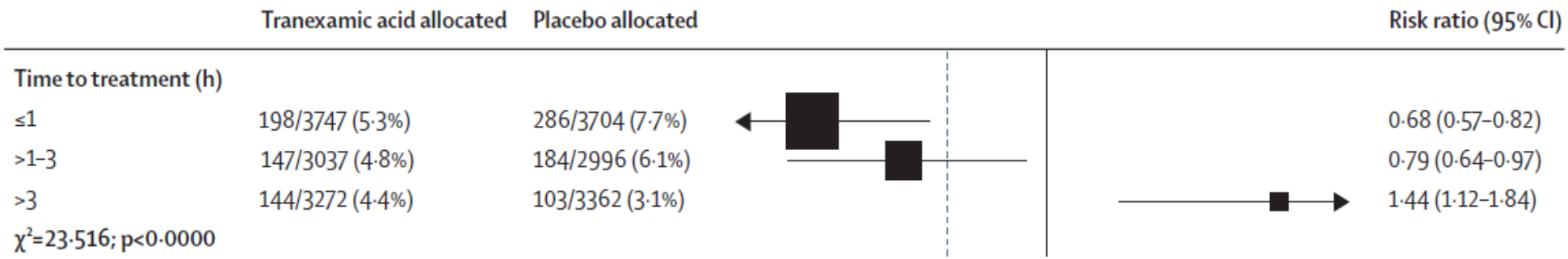
CRASH-2 Collaborators Lancet 2010;376:23-32

Trauma

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

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

Table 2: **Death by cause**



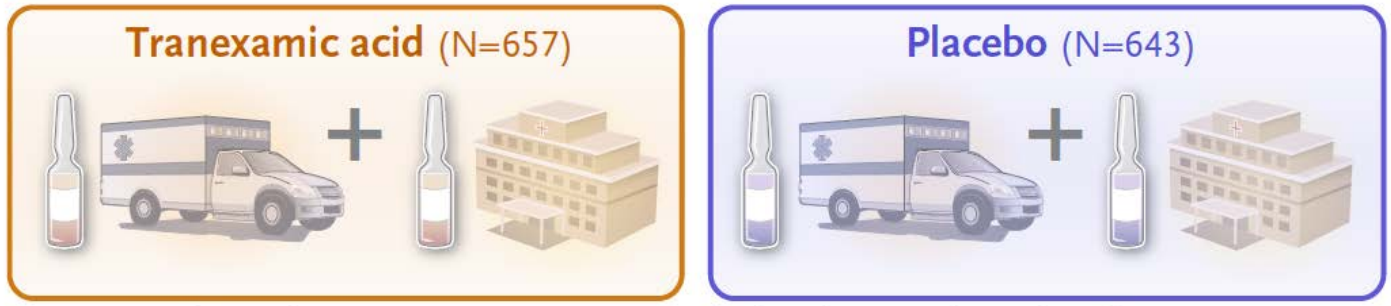
CRASH-2 Collaborators Lancet 2010;376:23-32

New Trauma Study

Prehospital Tranexamic Acid for Severe Trauma

The PATCH-Trauma Investigators and the ANZICS Clinical Trials Group*

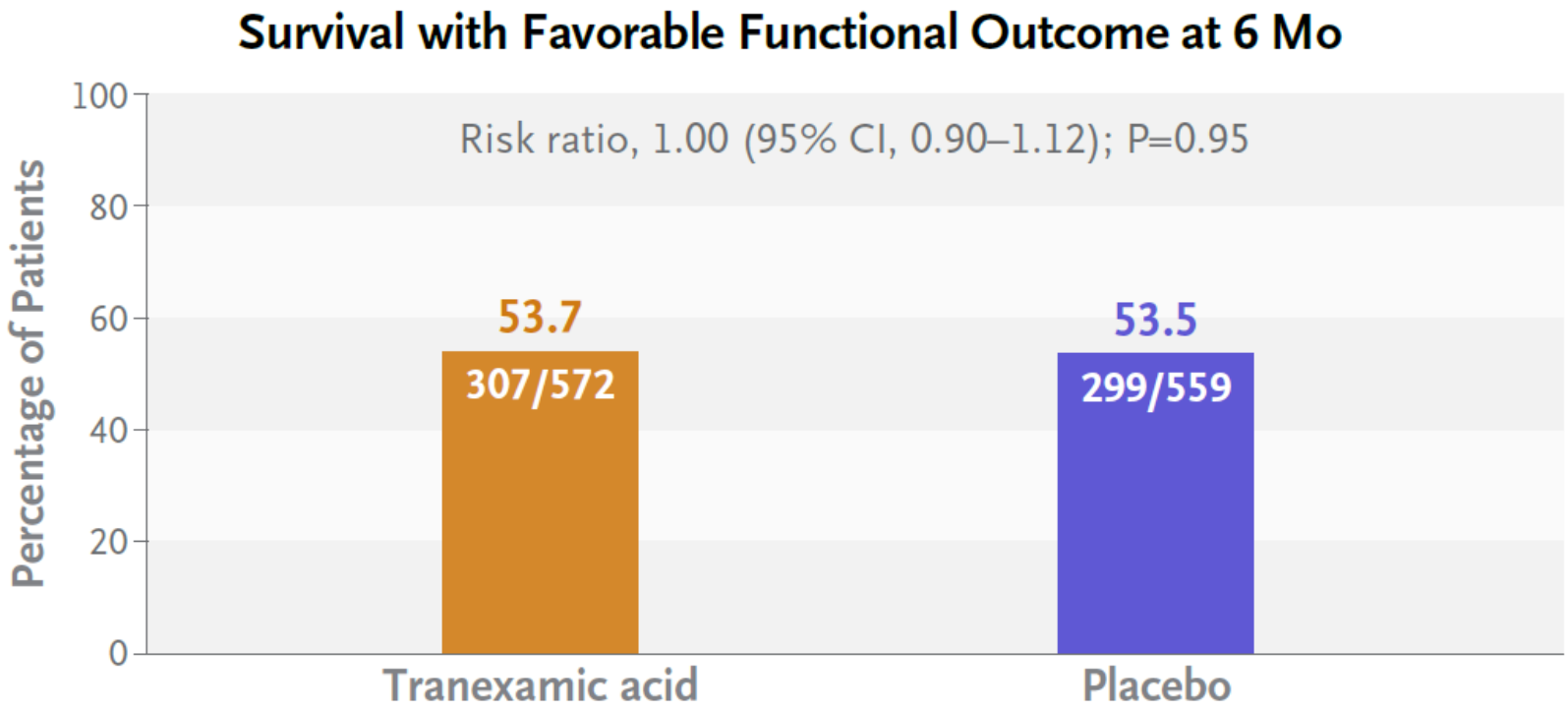
- Patients with severe injuries, at high risk for coagulopathy, care in advanced trauma systems



Before admission: 1-g intravenous bolus dose within 3 hr after injury
After admission: 1-g infusion over 8 hr

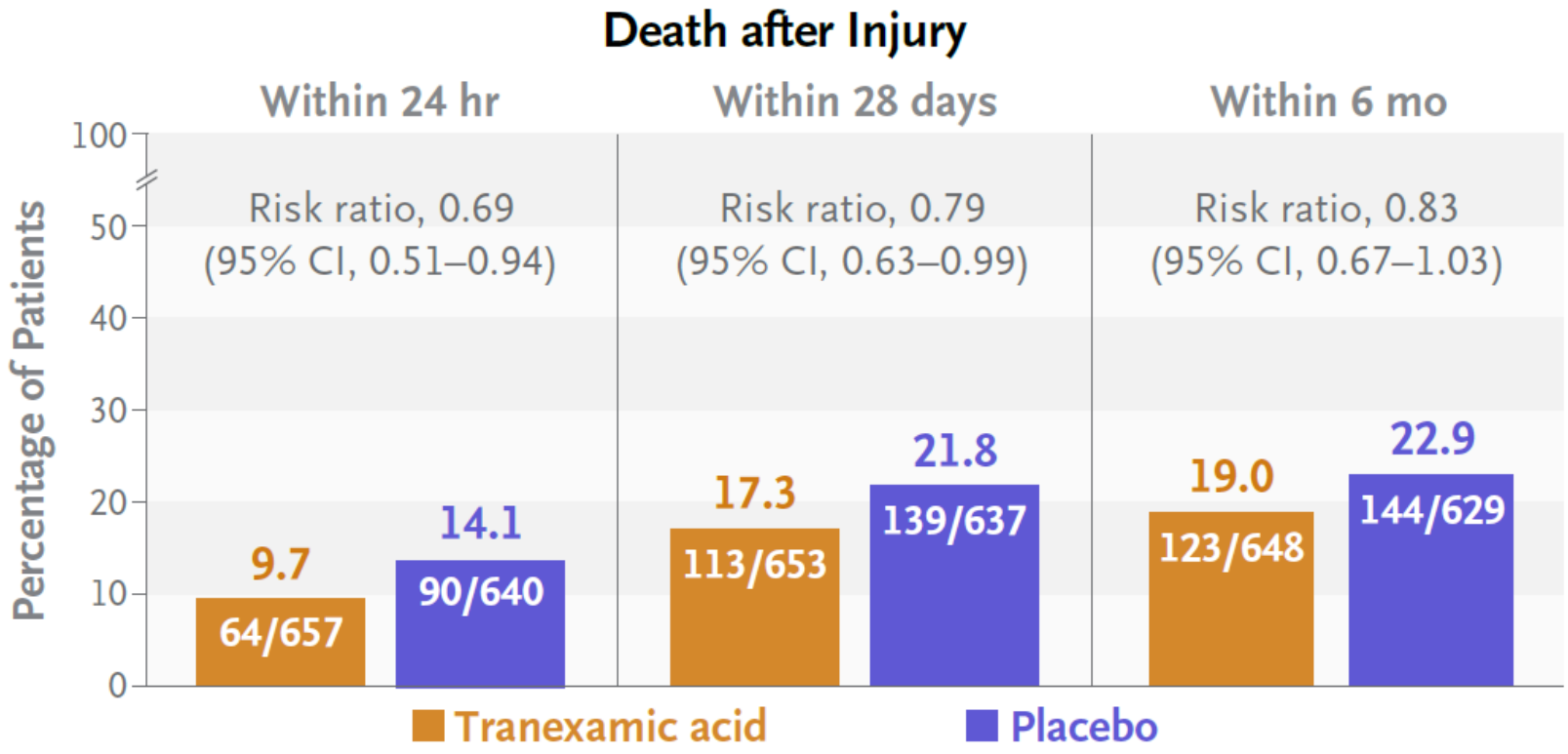
PATCH/ANZICS Groups NEJM 2023;389:127-136

Primary Outcome



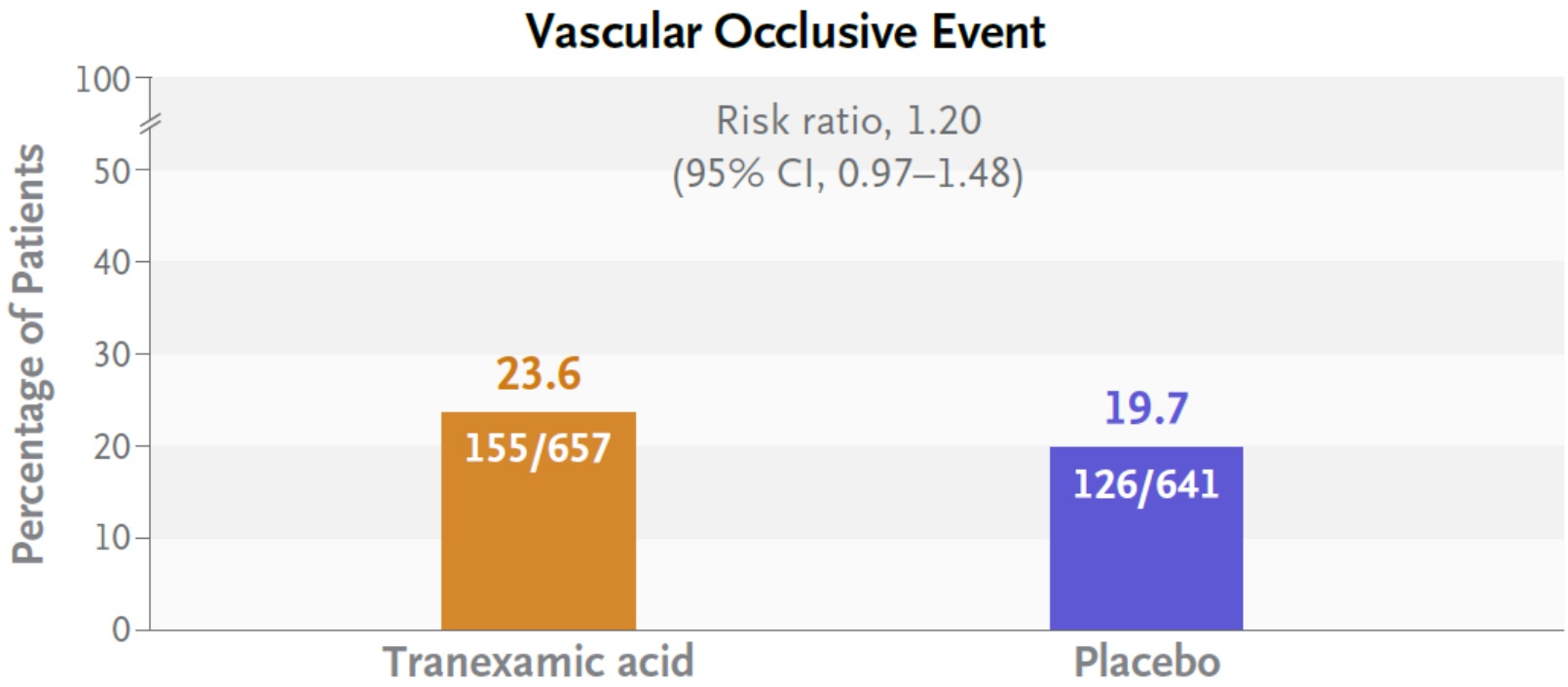
PATCH/ANZICS Groups NEJM 2023;389:127-136

Secondary Outcomes



PATCH/ANZICS Groups NEJM 2023;389:127-136

Safety



PATCH/ANZICS Groups NEJM 2023;389:127-136

Cardiac Surgery – High vs Low Dose

JAMA | Original Investigation

Effect of High- vs Low-Dose Tranexamic Acid Infusion on Need for Red Blood Cell Transfusion and Adverse Events in Patients Undergoing Cardiac Surgery

The OPTIMAL Randomized Clinical Trial

Jia Shi, MD; Chenghui Zhou, MD; Wei Pan, MD; Hansong Sun, MD; Sheng Liu, MD; Wei Feng, MD; Weijian Wang, MD; Zhaoyun Cheng, MD; Yang Wang, PhD; Zhe Zheng, MD; for the OPTIMAL Study Group

- N=3031
- High-dose ≈100 mg/kg vs Low-dose ≈ 20 mg/kg

Shi et al. JAMA 2022;328:336-347

Cardiac Surgery – High vs Low Dose

Table 2. Primary and Secondary Outcomes

Outcomes	High-dose tranexamic acid	Low-dose tranexamic acid	Estimate of difference (95% CI)	*P* value
Full analysis set, No.	1525	1506		
Primary efficacy end point				
Patients with red blood cell transfusion, No. (%)	333 (21.8)	391 (26.0)	−4.1 (−∞ to −1.1)[a]	.004
Adjusted for study site			−4.0 (−∞ to −1.0)[a]	.005
Primary safety end point				
30-d composite, No./total (%)	265/1502 (17.6)	249/1481 (16.8)	0.8 (−∞ to 3.9)[b]	.003
Adjusted for study site			0.9 (−∞ to 3.9)[b]	.004
Safety end-point components, No. (%)				
Clinical seizure[c]	15 (1.0)	6 (0.4)	0.6 (−0.0 to 1.2)	.05
Kidney dysfunction[d]	71 (4.7)	71 (4.7)	−0.1 (−1.6 to 1.5)	.94
Myocardial infarction[e]	172 (11.3)	167 (11.1)	0.2 (−2.1 to 2.5)	.87
Stroke[f]	10 (0.7)	8 (0.5)	0.1 (−0.5 to 0.7)	.66
Pulmonary embolism[g]	1 (0.1)	0	0.1 (−0.2 to 0.0)	>.99
Deep vein thrombosis[h]	15 (1.0)	12 (0.8)	0.2 (−0.5 to 0.9)	.58
Death[i]	9 (0.6)	10 (0.7)	−0.1 (−0.1 to 0.01)	.80

Shi et al. JAMA 2022;328:336-347

Non-Cardiac Surgery

Tranexamic Acid in Patients Undergoing Noncardiac Surgery

P.J. Devereaux, M. Marcucci, T.W. Painter, D. Conen, V. Lomivorotov,

- N=9535
- Non-cardiac surgery at-risk for bleeding but excluding neurosurgery or cases where physicians were planning on using tranexamic acid
- Dose: 1 g at start and 1g at end of surgery

Devereaux et al. NEJM 2022;386:1986-97

Non-Cardiac Surgery

Any procedure	4729/4757 (99.4)	4740/4778 (99.2)
General‡	1769/4729 (37.4)	1773/4740 (37.4)
Orthopedic	1083/4729 (22.9)	1063/4740 (22.4)
Vascular	699/4729 (14.8)	700/4740 (14.8)
Urologic	598/4729 (12.6)	624/4740 (13.2)
Spinal	237/4729 (5.0)	206/4740 (4.3)
Gynecologic	162/4729 (3.4)	171/4740 (3.6)
Thoracic	127/4729 (2.7)	146/4740 (3.1)
Low-risk	39/4729 (0.8)	34/4740 (0.7)
Plastic	14/4729 (0.3)	23/4740 (0.5)

Devereaux et al. NEJM 2022;386:1986-97

Non-Cardiac Surgery

Table 2. Effects of Tranexamic Acid on 30-Day Outcomes.*

Outcome	Tranexamic Acid (N=4757)	Placebo (N=4778)	Hazard Ratio (95% CI)†	P Value
Primary efficacy outcome: composite bleeding outcome — no. (%)‡	433 (9.1)	561 (11.7)	0.76 (0.67–0.87)	<0.001§
Individual components of composite bleeding outcome — no. (%)				
Life-threatening bleeding¶	78 (1.6)	79 (1.7)	0.99 (0.73–1.36)	
Major bleeding¶	363 (7.6)	496 (10.4)	0.72 (0.63–0.83)	
Bleeding into a critical organ¶	12 (0.3)	21 (0.4)	0.57 (0.28–1.16)	
Primary safety outcome: composite cardiovascular outcome — no./total no. (%)‖	649/4581 (14.2)	639/4601 (13.9)	1.02 (0.92–1.14)	0.04**
Individual components of composite cardiovascular outcome — no. (%)				
MINS¶	608 (12.8)	602 (12.6)	1.02 (0.91–1.14)	
Nonhemorrhagic stroke††	24 (0.5)	16 (0.3)	1.51 (0.80–2.84)	
Peripheral arterial thrombosis††	22 (0.5)	23 (0.5)	0.96 (0.53–1.72)	
Symptomatic proximal venous thromboembolism††	32 (0.7)	28 (0.6)	1.15 (0.69–1.91)	
Other secondary outcomes — no. (%)				
Bleeding independently associated with death after noncardiac surgery	416 (8.7)	541 (11.3)	0.76 (0.67–0.87)	
MINS not fulfilling the universal definition of myocardial infarction	549 (11.5)	549 (11.5)	1.01 (0.89–1.13)	
Myocardial infarction	67 (1.4)	53 (1.1)	1.27 (0.89–1.82)	
Net risk–benefit outcome‡‡	983 (20.7)	1046 (21.9)	0.94 (0.86–1.02)	

Devereaux et al. NEJM 2022;386:1986-97

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Hemorrhagic Stroke + PE	26 (0.5)	17 (0.4)		

3.6% vs 2.9% (P <0.05)

Devereaux et al. NEJM 2022;386:1986-97

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3.6% vs 2.9% (P <0.05)

Seizure n = 10 (0.2) versus 3 (0.1)

Devereaux et al. NEJM 2022;386:1986-97

GI Bleed

Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial

*The HALT-IT Trial Collaborators**

- N = 12,009
- Dose: 1 g + 3g/24 hours
- Primary outcome: 5-day bleeding mortality

HALT-IT Trial Collaborators Lancet 2020;395:1927-1936

GI Bleed

Outcome	TXA N=5994	Placebo N=6015	RR (95% CI)
Death due to bleeding within 5 d	3.7%	3.8%	0.99 (0.82-1.18)
Arterial TE (MI/CVA)	0.7%	0.8%	0.92 (0.60-1.39)
Venous TE Seizures	0.8% 0.6%	0.4% 0.4%	1.85 (1.15-2.98) 1.73 (1.03-2.93)
Transfusion	68.5%	69.1%	0.99 (0.97-1.02)

HALT-IT Trial Collaborators Lancet 2020;395:1927-1936

Does Tranexamic Acid Meet Adoption Criteria?

1. Is it effective? Yes

2. Is it as safe (or safer) than transfusion alternatives? Yes

3. Are the costs reasonable? Yes

- My recommendations:
  - Use for blood sparing effects prophylactically where indicated (e.g., cardiac surgery, orthopedic surgery) and selectively in high-blood-loss surgeries

Restrictive Transfusion Threshold

- Landmark study:

A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D., CLAUDIO MARTIN, M.D., GIUSEPPE PAGLIARELLO, M.D., MARTIN TWEEDDALE, M.D., PH.D., IRWIN SCHWEITZER, M.SC., ELIZABETH YETISIR, M.SC., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

- Euvolemic, non-bleeding patients with Hb $\leq$ 90 g/L within 72 hours of admission to ICU
  - Restrictive strategy: RBC if Hb < 70 g/L, to maintain at 70 - 90 g/L
  - Liberal strategy: RBC if Hb <100 g/L, to maintain at 100 - 120 g/L
- Results:
  - 54% reduction in transfusions
  - No difference in adverse outcomes

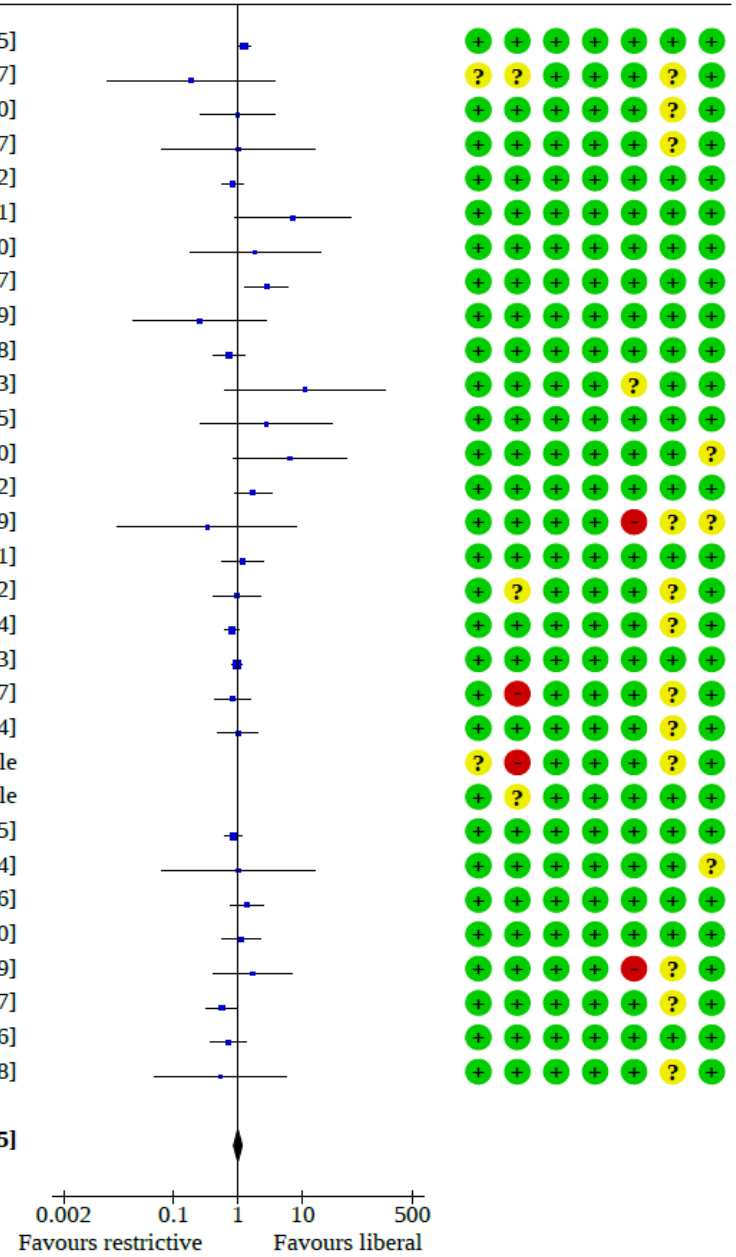
Hebert et al. NEJM 1999;340:409-417

Analysis 1.1. Comparison 1: Mortality at 30 days, Outcome 1: 30-Day mortality

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
Bergamin 2017	84	151	67	149	11.8%	1.24 [0.99 , 1.55]
Blair 1986	0	26	2	24	0.2%	0.19 [0.01 , 3.67]
Bush 1997	4	50	4	49	1.1%	0.98 [0.26 , 3.70]
Carson 1998	1	42	1	42	0.3%	1.00 [0.06 , 15.47]
Carson 2011	43	1009	52	1007	7.4%	0.83 [0.56 , 1.22]
Carson 2013	7	55	1	55	0.5%	7.00 [0.89 , 55.01]
Cooper 2011	2	23	1	21	0.4%	1.83 [0.18 , 18.70]
de Almeida 2015	23	101	8	97	3.0%	2.76 [1.30 , 5.87]
DeZern 2016	1	59	2	30	0.4%	0.25 [0.02 , 2.69]
Ducrocq 2021	19	342	25	324	4.6%	0.72 [0.40 , 1.28]
Foss 2009	5	60	0	60	0.2%	11.00 [0.62 , 194.63]
Gillies 2020	2	26	1	36	0.4%	2.77 [0.26 , 28.95]
Gobatto 2019	7	23	1	21	0.5%	6.39 [0.86 , 47.70]
Gregersen 2015	21	144	12	140	3.6%	1.70 [0.87 , 3.32]
Grover 2006	0	109	1	109	0.2%	0.33 [0.01 , 8.09]
Hajjar 2010	15	249	13	253	3.2%	1.17 [0.57 , 2.41]
Hébert 1995	8	33	9	36	2.6%	0.97 [0.42 , 2.22]
Hébert 1999	78	418	98	420	10.7%	0.80 [0.61 , 1.04]
Holst 2014	168	502	175	496	13.5%	0.95 [0.80 , 1.13]
Jairath 2015	14	257	25	382	4.0%	0.83 [0.44 , 1.57]
Lacroix 2007	14	320	14	317	3.2%	0.99 [0.48 , 2.04]
Laine 2018	0	40	0	40		Not estimable
Lotke 1999	0	62	0	65		Not estimable
Mazer 2017	74	2427	87	2429	9.6%	0.85 [0.63 , 1.15]
Møller 2019	1	29	1	29	0.3%	1.00 [0.07 , 15.24]
Murphy 2015	26	1000	19	1003	4.5%	1.37 [0.76 , 2.46]
Palmieri 2017	16	168	15	177	3.6%	1.12 [0.57 , 2.20]
Parker 2013	5	100	3	100	1.0%	1.67 [0.41 , 6.79]
Villanueva 2013	19	416	34	417	5.0%	0.56 [0.32 , 0.97]
Walsh 2013	12	51	16	49	3.9%	0.72 [0.38 , 1.36]
Webert 2008	1	29	2	31	0.4%	0.53 [0.05 , 5.58]
Total (95% CI)		**8321**		**8408**	**100.0%**	**0.99 [0.86 , 1.15]**
Total events:	670		689			

Heterogeneity: Tau² = 0.03; Chi² = 40.06, df = 28 (P = 0.07); I² = 30%

Test for overall effect: Z = 0.07 (P = 0.94)

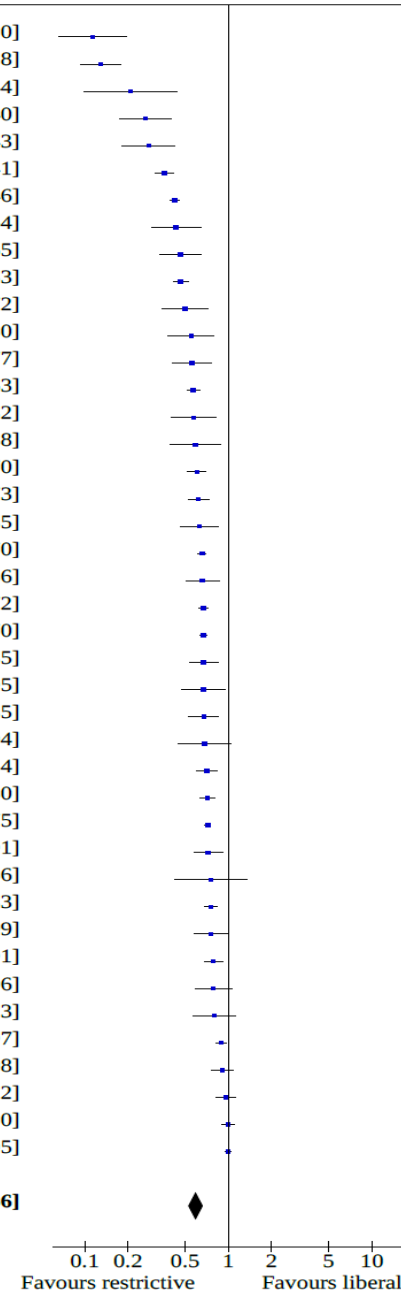


Analysis 6.1. Comparison 6: Blood transfusions, Outcome 1: Participants exposed to blood transfusion (all trials

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
Parker 2013	11	100	100	100	1.6%	0.11 [0.07 , 0.20]
Prick 2014	33	261	251	258	2.2%	0.13 [0.09 , 0.18]
Blair 1986	5	26	24	24	1.1%	0.21 [0.10 , 0.44]
Lotke 1999	16	62	65	65	1.9%	0.26 [0.17 , 0.40]
Carson 2013	15	55	55	55	1.9%	0.28 [0.18 , 0.43]
Ducrocq 2021	122	342	323	324	2.7%	0.36 [0.31 , 0.41]
Carson 2011	415	1009	974	1007	2.8%	0.43 [0.39 , 0.46]
Gillies 2020	15	36	25	26	2.0%	0.43 [0.29 , 0.64]
Carson 1998	19	42	41	42	2.2%	0.46 [0.33 , 0.65]
Lacroix 2007	146	320	310	317	2.7%	0.47 [0.41 , 0.53]
Foss 2009	22	60	44	60	2.1%	0.50 [0.35 , 0.72]
Cooper 2011	13	24	21	21	2.1%	0.55 [0.38 , 0.80]
Hébert 1995	18	33	35	36	2.2%	0.56 [0.41 , 0.77]
Villanueva 2013	219	444	384	445	2.8%	0.57 [0.52 , 0.63]
Gobatto 2019	13	23	21	21	2.1%	0.58 [0.40 , 0.82]
Shehata 2012	13	25	22	25	2.0%	0.59 [0.39 , 0.88]
Hajjar 2010	118	249	198	253	2.7%	0.61 [0.52 , 0.70]
Tay 2020	80	150	129	150	2.6%	0.62 [0.53 , 0.73]
Laine 2018	22	40	35	40	2.3%	0.63 [0.46 , 0.85]
Holst 2014	326	502	490	496	2.8%	0.66 [0.62 , 0.70]
Møller 2019	19	29	29	29	2.4%	0.66 [0.51 , 0.86]
Hébert 1999	280	418	420	420	2.8%	0.67 [0.63 , 0.72]
Murphy 2015	637	1000	952	1003	2.8%	0.67 [0.64 , 0.70]
Bergamin 2017	62	151	91	149	2.5%	0.67 [0.53 , 0.85]
de Almeida 2015	33	101	47	97	2.1%	0.67 [0.48 , 0.95]
So-Osman 2013	79	299	119	304	2.5%	0.67 [0.53 , 0.85]
Topley 1956	8	12	10	10	1.9%	0.68 [0.45 , 1.04]
Jairath 2015	133	403	247	533	2.6%	0.71 [0.60 , 0.84]
Koch 2017	195	363	265	354	2.7%	0.72 [0.64 , 0.80]
Mazer 2017	1271	2430	1765	2430	2.8%	0.72 [0.69 , 0.75]
Bracey 1999	74	212	104	216	2.5%	0.72 [0.58 , 0.91]
Nielsen 2014	11	30	16	33	1.5%	0.76 [0.42 , 1.36]
Gregersen 2015	109	144	140	140	2.8%	0.76 [0.69 , 0.83]
Johnson 1992	15	20	18	18	2.4%	0.76 [0.58 , 0.99]
Walsh 2013	40	51	49	49	2.7%	0.79 [0.68 , 0.91]
Fan 2014	41	96	52	96	2.3%	0.79 [0.59 , 1.06]
Grover 2006	37	109	46	109	2.2%	0.80 [0.57 , 1.13]
Palmieri 2017	141	168	166	177	2.8%	0.89 [0.83 , 0.97]
Bush 1997	40	50	43	49	2.6%	0.91 [0.77 , 1.08]
Webert 2008 (1)	26	29	29	31	2.7%	0.96 [0.82 , 1.12]
Stanworth 2020	20	20	18	18	2.8%	1.00 [0.91 , 1.10]
DeZern 2016	59	59	30	30	2.8%	1.00 [0.95 , 1.05]
Total (95% CI)		**9997**		**10060**	**100.0%**	**0.59 [0.53 , 0.66]**
Total events:	4971		8203			

Heterogeneity: Tau² = 0.10; Chi² = 1104.24, df = 41 (P < 0.00001); I² = 96%

Test for overall effect: Z = 9.93 (P < 0.00001)



The MINT Study

Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia

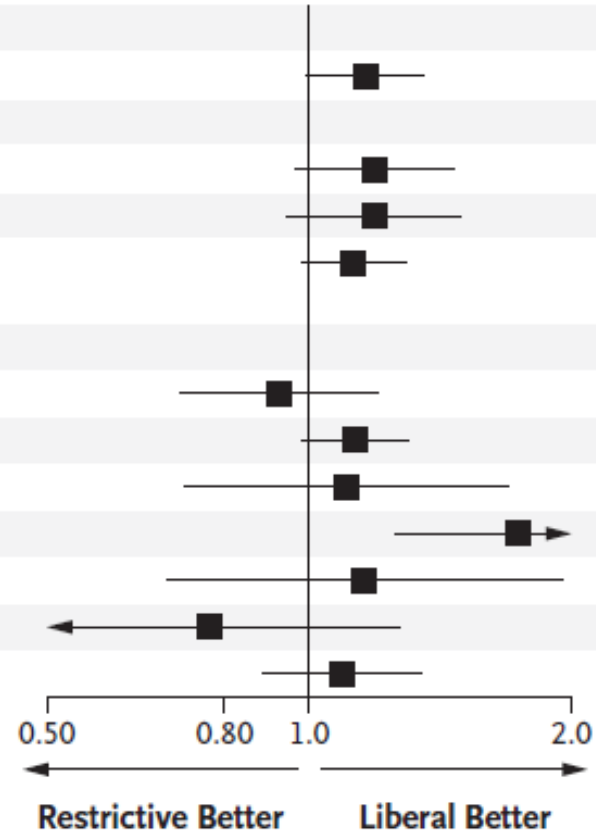
J.L. Carson, M.M. Brooks, P.C. Hébert, S.G. Goodman, M. Bertolet, S.A. Glynn, B.R. Chaitman, T. Simon, R.D. Lopes, A.M. Goldsweig, A.P. DeFilippis, J.D. Abbott, B.J. Potter, F.M. Carrier, S.V. Rao, H.A. Cooper, S. Ghafghazi, D.A. Fergusson, W.J. Kostis, H. Noveck, S. Kim, M. Tessalee, G. Ducrocq, P. Gabriel Melo de Barros e Silva, D.J. Triulzi, C. Alsweiler, M.A. Menegus, J.D. Neary, L. Uhl, J.B. Strom, C.B. Fordyce, E. Ferrari, J. Silvain, F.O. Wood, B. Daneault, T.S. Polonsky, M. Senaratne, E. Puymirat, C. Bouleti, B. Lattuca, H.D. White, S.F. Kelsey, P.G. Steg, and J.H. Alexander, for the MINT Investigators*

- Liberal (<100 g/L) vs. restrictive (<70-80 g/L) transfusion strategy in patients with acute MI

Carson et al. NEJM 2023;389:2446-2456

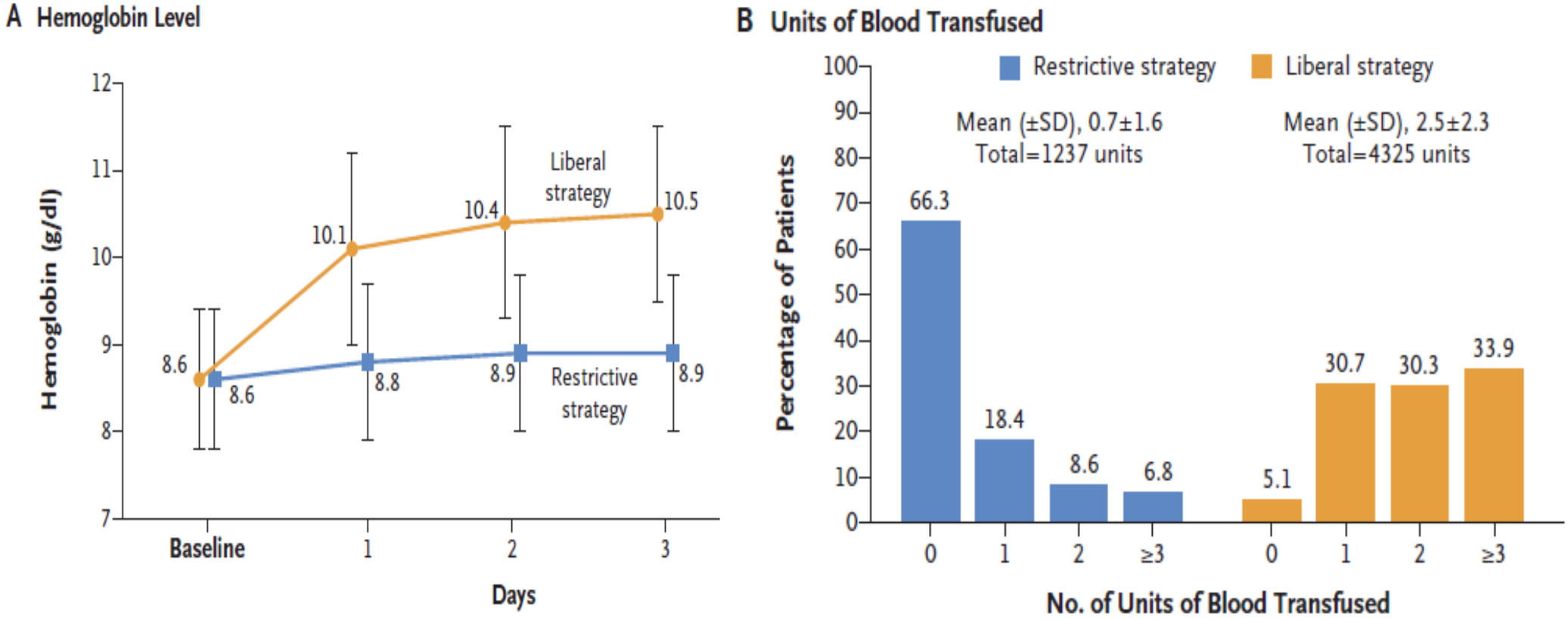
Results

Outcome	Restrictive Strategy	Liberal Strategy	Risk Ratio (95% CI)
	no. of patients/total no. (%)		
Primary outcome			
Myocardial infarction or death	295/1749 (16.9)	255/1755 (14.5)	1.16 (1.00–1.35)
Secondary outcomes			
Death	173/1749 (9.9)	146/1755 (8.3)	1.19 (0.96–1.47)
Myocardial infarction	149/1749 (8.5)	126/1755 (7.2)	1.19 (0.94–1.49)
Death, myocardial infarction, revascularization, or rehospitalization	342/1749 (19.6)	305/1755 (17.4)	1.13 (0.98–1.29)
Other outcomes			
Heart failure	102/1749 (5.8)	111/1755 (6.3)	0.92 (0.71–1.20)
Death, myocardial infarction, or unstable angina	338/1749 (19.3)	300/1755 (17.1)	1.13 (0.98–1.30)
Unscheduled revascularization	43/1749 (2.5)	39/1755 (2.2)	1.11 (0.72–1.70)
Cardiac death	97/1749 (5.5)	56/1755 (3.2)	1.74 (1.26–2.40)
Stroke	30/1749 (1.7)	26/1755 (1.5)	1.16 (0.69–1.95)
Pulmonary embolism or deep venous thrombosis	26/1749 (1.5)	34/1755 (1.9)	0.77 (0.46–1.27)
Pneumonia or bacteremia	166/1749 (9.5)	153/1755 (8.7)	1.09 (0.88–1.34)



Carson et al. NEJM 2023;389:2446-2456

Results



Carson et al. NEJM 2023;389:2446-2456

Considerations

- Primary outcome was not statistically significant
- Outcome assessors not blinded; Cardiac death not adjudicated
- No adjustment for multiple comparisons
- About 35% received RBC transfusions before randomization
- Imbalance in protocol discontinuation
  - Restrictive: 46/1749 patients (3%)
    - n=24 for clinical reasons, including surgery and bleeding
  - Liberal: 241/1755 patients (14%)
    - N=89 for clinical reasons, including adverse effects, fluid overload
    - N=121 due to patient or provider preference
    - N=31 for other reasons, including blood supply shortages

Interpretation

- MINT is a negative study
- >30 negative studies showing that a restrictive transfusion strategy does not increase risk of adverse outcomes in studied groups
- Generalizability is limited to studied groups
  - Bleeding or symptomatic patients are typically excluded
    - Acute infarct can be considered a symptom of severe anemia and should be treated
  - Many surgical patients need higher hemoglobin levels because of:
    - Bleeding or coagulopathy
    - Unstable or dynamic fluid status
  - Critically ill with limited organ reserve

- Transfusion decision more complicated than just measuring Hb level
- Adopting a liberal transfusion strategy would preclude us from using what's arguably the most effective blood conservation strategy

Does Restrictive RBC Transfusion Strategy Meet Adoption Criteria?

1. Is it effective? Yes
2. Is it as safe (or safer) than transfusion alternatives? Yes
3. Are the costs reasonable? Yes

- My Recommendations:
  - Use during surgery as long as there are no clinical indications for higher hemoglobin levels (i.e., do not change practice because of MINT study)

POC-Guided, Targeted Hemostatic Therapy

Point-of-Care Hemostatic Testing in Cardiac Surgery

A Stepped-Wedge Clustered Randomized Controlled Trial

- N = 7402
  - 3555 control
  - 3847 intervention

Group 6 N=2 Hospitals	n=144	n=140	n=150	n=132	n=130	n=168	n=114
Group 5 N=2 Hospitals	n=192	n=197	n=227	n=214	n=211	n=258	n=203
Group 4 N=2 Hospitals	n=189	n=175	n=183	n=178	n=171	n=209	n=135
Group 3 N=2 Hospitals	n=136	n=121	n=122	n=136	n=115	n=146	n=135
Group 2 N=2 Hospitals	n=172	n=170	n=171	n=174	n=164	n=214	n=170
Group 1 N=2 Hospitals	n=204	n=220	n=216	n=220	n=214	n=250	n=212
Total (n=7402)	**n=1037**	**n=1023**	**n=1069**	**n=1054**	**n=1005**	**n=1245**	**n=969**
Period	**Baseline** Oct 1 2014– Nov 2 2014	**Step 1** Nov 3 2014 – Nov 30 2014	**Step 2** Dec 1 2014 – Jan 4 2015	**Step 3** Jan 5 2015 – Feb 1 2015	**Step 4** Feb 2 2015 – Mar 1 2015	**Step 5** Mar 2 2015 – Apr 5 2015	**Follow-up** Apr 6 2015 – May 1, 2015

Karkouti et al. Circulation 2016;134:1152-1162

Results

Outcome	Relative Risk Reduction
RBC	0.91 (0.85 – 0.98); P = 0.02; NNT = 24.7
Platelet	0.77 (0.68 – 0.87); P < 0.001; NNT = 16.7
Plasma	NC
Cryoprecipitate	NC
Major Bleeding	0.83 (0.72 – 0.94); P = 0.004; NNT = 22.6
Adverse Outcomes	NC
Processes of Care	NC

Karkouti et al. Circulation 2016;134:1152-1162

Does POC-Guided, Targeted Hemostatic Therapy Meet Adoption Criteria?

1. Is it effective? Yes
2. Is it as safe (or safer) than transfusion alternatives? Yes
3. Are the costs reasonable? Yes

- My Recommendations:
  - Use in bleeding patients in favour of ratio-based transfusion management

Summary

- Recent PBM Update:

GUIDELINE TITLE STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management

RELEASE DATE June 30, 2021

PRIOR VERSIONS 2011 (update), 2007

DEVELOPER Society of Thoracic Surgeons (STS), Society of Cardiovascular Anesthesiologists (SCA), American Society of ExtraCorporeal Technology (AmSECT), and Society for the Advancement of Blood Management (SABM)

TARGET POPULATION Adult cardiothoracic and other high-risk surgical patients

MAJOR RECOMMENDATIONS

- Use of synthetic antifibrinolytic agents such as ε-aminocaproic acid or tranexamic acid is indicated for blood conservation in surgery (strong recommendation; strong evidence).
- A restrictive perioperative allogeneic packed red blood cell transfusion strategy is preferred over a liberal strategy to conserve blood (strong recommendation; strong evidence).
- Goal-directed transfusion algorithms incorporating point-of-care testing are recommended to reduce periprocedural bleeding and transfusion (strong recommendation; moderate evidence).
- For elective cases, ticagrelor should be withdrawn preoperatively for a minimum of 3 days, clopidogrel for 5 days, and prasugrel for 7 days (strong recommendation; moderate evidence).

Hameed et al. JAMA 2022;327:578-579

Thank you