Queen's UNIVERSITY

RBC Transfusion

Science not the Art of Medicine

Transfusion Camp: September 2021

Disclosure

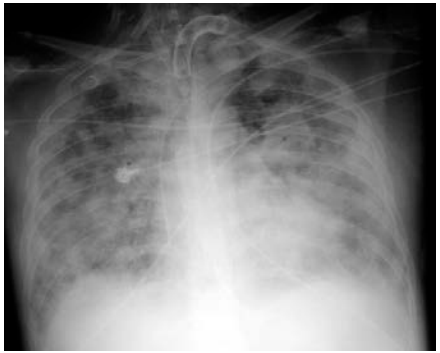
- Research funding from CSL Behring, Octapharma, Defense Research and Development Canada, CIHR, Heart and Stroke, and Canadian Blood Services

Outline

- **2 Cases**
- **RBC Basics**
- **Key risks of RBCs**
- **When should you give RBCs?**
  - Multiple randomized trials and meta-analyses to guide your decisions

[Note: massive hemorrhage, outpatient transfusions, and pediatric guidelines will be covered later/elsewhere]

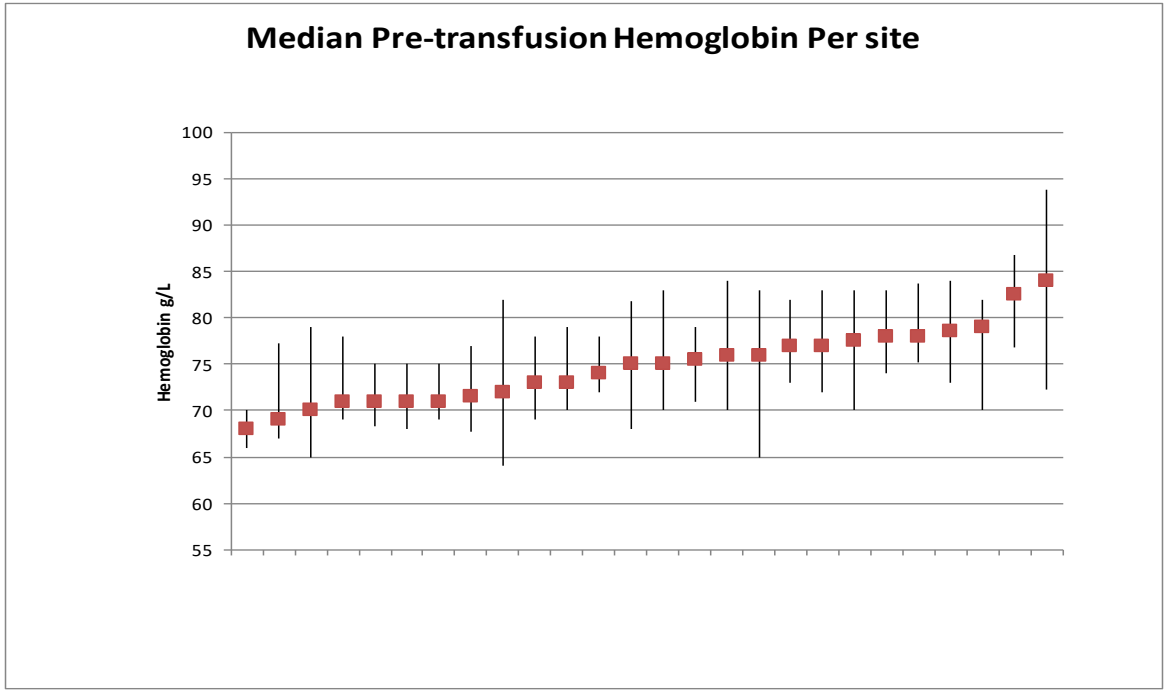
Why is it important that we use RBCs appropriately?



Adverse reactions

Supply and donor iron deficiency

Transfusion Practice is Highly Variable



Case 1

- 27 year old female, 4 days post C-section complicated by moderate PPH. Pre-delivery hemoglobin was 105 g/L. Hemoglobin this morning is 57 g/L. Heart rate 87. BP 102/56. She is pale and tired. No pre-syncope or lightheadedness. You have ordered a dose of intravenous iron. Plan is for discharge today.
- Should you transfuse RBCs?

Case 2

- 76 year old woman 4 days post-op from a spontaneous hip fracture surgery. Plan to discharge to rehab tomorrow. Hemoglobin 71 g/L. Asymptomatic. Vitals stable. No cardiac history.
- Should you transfuse RBCs?

RBC Basics

- Regular
  - Volume 300 mL, hematocrit 50-65%, SAG-M
  - Each unit increases hemoglobin by 10 g/L
  - Residual plasma – 2-30 mL
  - Acceptable for transfusion for 42 days from donation
- Irradiated
  - For immunocompromised patients at risk of TA-GVHD
  - More potassium load and free hemoglobin
- CMV-negative*

*The Canadian National Advisory Committee on Blood–IUT only

PATIENTS REQUIRING IRRADIATED BLOOD[129]

- Patients with severe T-cell congenital immunodeficiency states
- Intrauterine transfusions (IUT)
- Neonatal exchange transfusions for infants with prior IUT
- Neonatal top-up transfusion if there has been a previous IUT
- Patients with Hodgkin's lymphoma
- Patients undergoing bone marrow or stem cell transplants
  - It is reasonable to continue providing irradiated products until immunosuppression discontinued
- Recipients of directed transfusions from family members
- Recipients of HLA-matched platelets
- Patients treated with purine analogs (e.g., fludarabine), purine antagonists (e.g., bendamustine), alemtuzumab and anti-thymocyte globulin

Pg. 71
Bloody Easy 4

[More on transfusion complications on day 2]

http://www.bcshguidelines.com/documents/irrad_bcsh_072010.pdf

The risks of RBCs

There is a potential risk for all patients

Risks of RBCs

- Transfusion associated circulatory overload (TACO) – 1in 50 to 1 in100
  - *300 mL of RBCs is not the same as 300 mL of saline*
- Transfusion-related acute lung injury (TRALI) – 1 in 10,000
- Acute and delayed hemolytic transfusion reactions
  - ABO-immune hemolysis (by mistake) – 1 in 40,000
  - RBC alloantibodies 1 in 13 (HDFN risk for girls and young women)
  - Delayed hemolytic transfusion reactions 1 in 7000
- Anaphylaxis – 1 in 20,000
- More bleeding (from GI bleeding trials)
- HLA alloimmunization (leading to long waits for organ transplants)
- Concern about a higher death rate with liberal transfusion practices (90-100 g/L triggers)

It's not because of a worry about HIV

<1 in 1,000,000	Transmission of West Nile Virus
1 in 4,000,000	Transmission of Chagas disease per unit of component
1 in 7,500,000	Transmission of hepatitis B virus per unit of component
1 in 7,600,000	Transmission of HTLV per unit of component
1 in 13,000,000	Transmission of hepatitis C virus per unit of component
1 in 21,000,000	Transmission of human immunodeficiency virus (HIV) per unit of component

Bloody easy 4, Ontario Transfusion Handbook, 2016.

TACO

- Rate of TACO increases with increasing age:
  - aged 80 yr+: 7.4%
  - aged 70-79 yr: 5.2%
  - aged 60-69 yr: 4.2%
  - aged 50-59 yr: 3.3%
  - aged 49 yr or less: 2.0%
- Increased rate of TACO with increasing amount of volume transfused ($P<0.001$) and increasing total fluid balance ($P<0.001$)
- Odds ratio of death for TACO cases compared with transfused controls of 3.8 (95% CI, 2.2 to 6.7) ($P<0.001$)

Leanne Clifford et al. Anesthesiology. 2015 January ; 122(1): 21–28.

Pre-transfusion RBC checklist

Red Blood Cell Pre-Transfusion Checklist

Alternatives failed or have been ordered?	❑ Anemia investigations completed (e.g., CBC, blood film, ferritin, iron saturation, vitamin B12, reticulocyte count) ❑ Iron (oral and IV), vitamin B12, erythropoietin ordered or not indicated
Consent?	Patient advised of risks of: ❑ TACO 1 in 100 ❑ Hemolytic reaction 1 in 7,000 ❑ TRALI 1 in 10,000 ❑ Major allergic reaction 1 in 40,000 ❑ Bacterial infection 1 in 250,000

Back of blood easy 4

Tseng, et al. 2016 Apr;26(2):104-10. doi: 10.1111/tme.12284. Epub 2016 Feb 10.

Pre-transfusion RBC Checklist

Female under 45?	❑ Order Kell-negative units ❑ Inform recipient of the potential risk of transfusion causing hemolytic disease of the newborn in future pregnancies
At risk for FATAL transfusion-associated Graft vs. Host Disease?	Order irradiated blood if patient has any history of the following: ❑ Hodgkin's lymphoma ❑ Allogeneic or autologous stem cell transplant ❑ Ever treated with fludarabine, cladribine, bendamustine, alemtuzumab, anti-thymocyte globulin (ATG) ❑ Congenital immunodeficiencies

Pre-transfusion RBC Checklist

Diuretics?

Does my patient have a history of:

- ❑ Age greater ≥70 years
- ❑ Renal dysfunction
- ❑ Left ventricular dysfunction
- ❑ Prior or current CHF
- ❑ Severe euvolemic anemia (hemoglobin <50 g/L)

- ❑ **If YES to any of the above:** prescribe PO/IV furosemide pre-transfusion (*unless currently hypovolemic*)

Rate and Dose?

- ❑ Specify rate of infusion (default rate is over 2 hours per unit; inpatients and patients at risk for TACO (need diuretics) infuse over 3-4 hours)
- ❑ Order 1 unit at a time (unless bleeding)

The donor

- Remember your responsibility to the donor when you prescribe blood

TABLE 3. Number and percent of donors with low ferritin and mean number of donations by sex and Hb level*

Sex	Hb (g/L)	Number of donors tested†	Ferritin (μg/L)	Donors with low ferritin (<25 μg/L)‡	Number of donations in past 12 months§
Female	125-129	889	26 (23-29)	586 (65.9)	1.7 (1.6-1.8)
	≥130	4734	33 (32-34)	2452 (51.8)	1.5 (1.5-1.6)
Male	125-129	173	36 (29-42)	98 (56.6)	3.3 (3.1-3.6)
	≥130	6762	64 (62-66)	2208 (32.7)	2.3 (2.3-2.4)

Goldman M, et al. Transfusion 2017 Mar;57(3):564-570.

Effects of iron deficiency

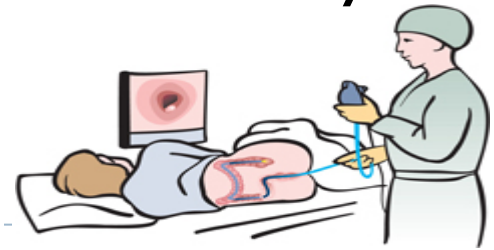
Concentration

Low birth weight infant

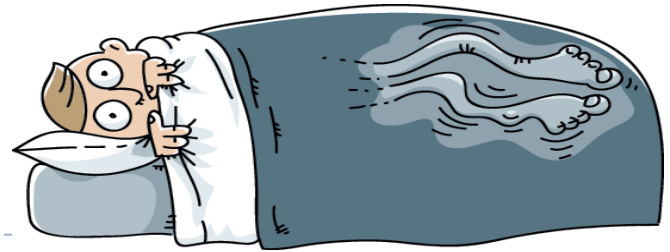
Fitness

Sadness

Unnecessary tests



Restless legs



Science not the "Art of Medicine"

- 34 RCTs with 22,943 patients
  - restrictive (70-75-80) vs. liberal (90-95-100)

Pre-TRICC

Hebert P, et al. Am J Resp CCM 1997; 155: 1618-23

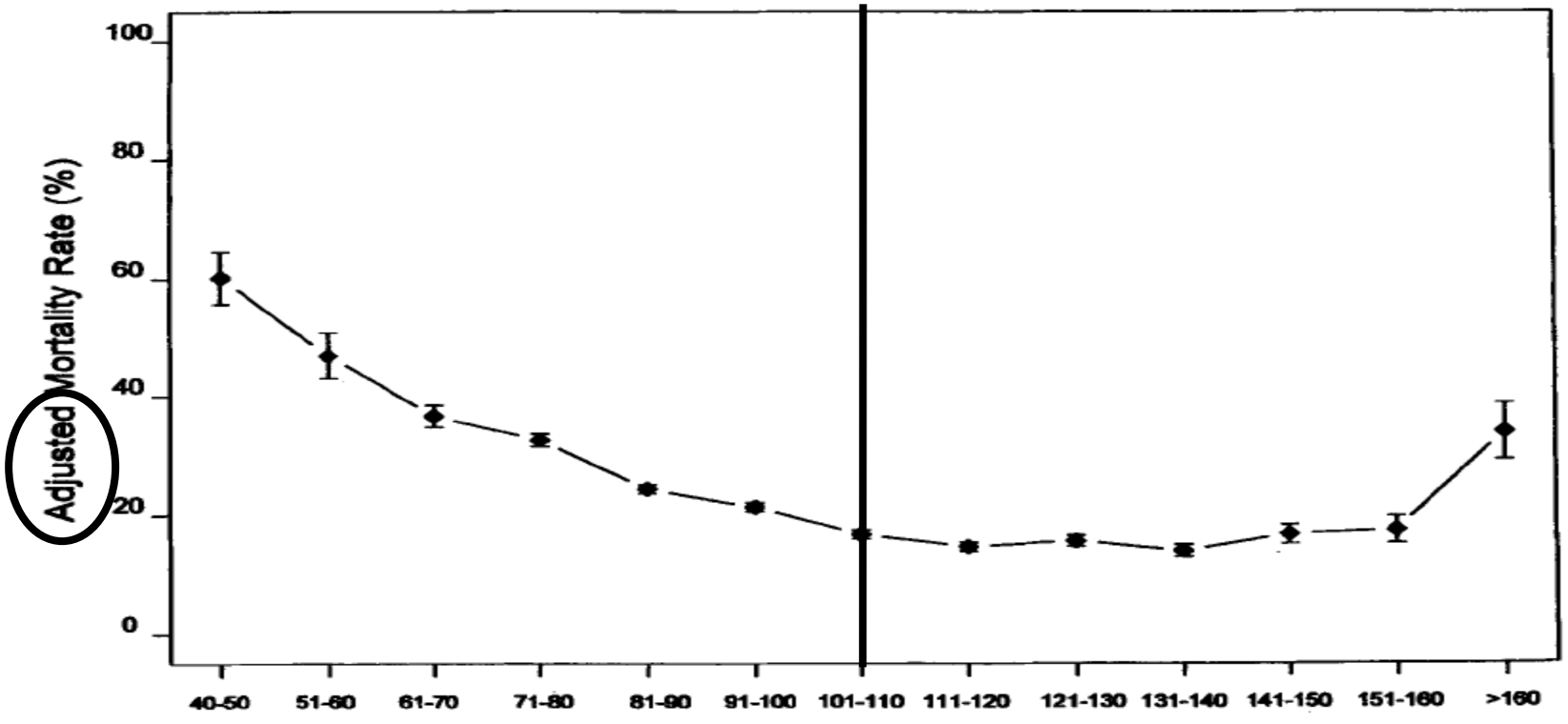
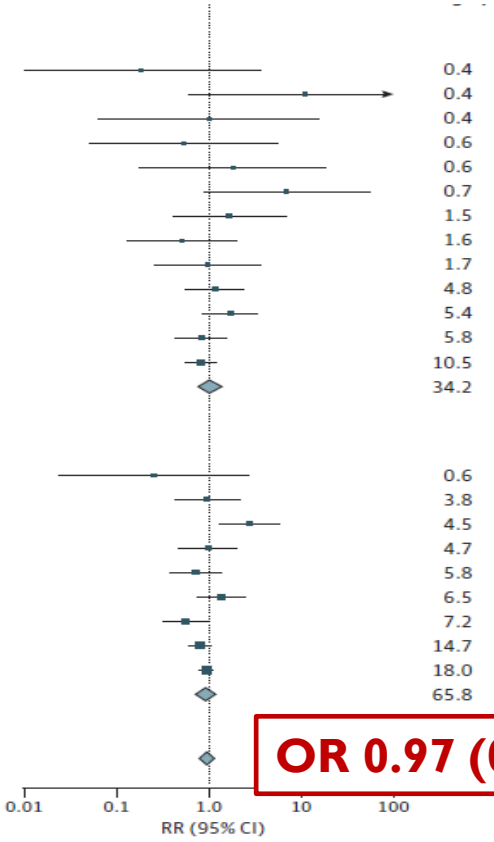


Figure 1. Comparison of 30-Day Mortality Using Restrictive vs Liberal Hemoglobin Transfusion Thresholds in Randomized Clinical Trials

JAMA 2016 Nov 15;316(19):2025-2035.

Source	Restrictive Transfusion Threshold: No. of Deaths	Restrictive Transfusion Threshold: Total No.	Liberal Transfusion Threshold: No. of Deaths	Liberal Transfusion Threshold: Total No.	RR (95
Restrictive threshold, hemoglobin <8 to 9 g/dL					
Lotke et al,[75] 1999	0	62	0	65	Not estimable
Blair et al,[53] 1986	0	26	2	24	0.19 (0.01-3.67)
Foss et al,[63] 2009	5	60	0	60	11.00 (0.62-194.63)
Carson et al,[58] 1998	1	42	1	42	1.00 (0.06-15.47)
Webert et al,[86] 2008	1	29	2	31	0.53 (0.05-5.58)
Cooper et al,[61] 2011	2	23	1	21	1.83 (0.18-18.70)
Carson et al,[56] 2013	7	55	1	55	7.00 (0.89-55.01)
Parker,[78] 2013	5	100	3	100	1.67 (0.41-6.79)
Bracey et al,[54] 1999	3	215	6	222	0.52 (0.13-2.04)
Bush et al,[55] 1997	4	50	4	49	0.98 (0.26-3.70)
Hajjar et al,[68] 2010	15	249	13	253	1.17 (0.57-2.41)
Gregersen et al,[64] 2015	21	144	12	140	1.70 (0.87-3.32)
Jairath et al,[72] 2015	14	257	25	382	0.83 (0.44-1.57)
Carson et al,[60] 2011	43	1009	52	1007	0.83 (0.56-1.22)
Subtotal	121	2321	122	2451	1.05 (0.78-1.40)
Heterogeneity: $\tau^2 = 0.02$; $\chi^2_{12} = 13.14$; $P = .36$; $I^2 = 9\%$					
Tests for overall effect: z score = 0.31; $P = .76$					
Restrictive threshold, hemoglobin <7 g/dL					
DeZern et al,[87] 2016	1	59	2	30	0.25 (0.02-2.69)
Hébert et al,[70] 1995	8	33	9	36	0.97 (0.42-2.22)
de Almeida et al,[79] 2015	23	101	8	97	2.76 (1.30-5.87)
Lacroix et al,[74] 2007	14	320	14	317	0.99 (0.48-2.04)
Walsh et al,[85] 2013	12	51	16	49	0.72 (0.38-1.36)
Murphy et al,[76] 2015	26	1000	19	1003	1.37 (0.76-2.46)
Villanueva et al,[84] 2013	19	416	34	417	0.56 (0.32-0.97)
Hébert et al,[69] 1999	78	418	98	420	0.80 (0.61-1.04)
Holst et al,[71] 2014	168	502	175	496	0.95 (0.80-1.13)
Subtotal	349	2900	375	2865	0.94 (0.74-1.19)
Heterogeneity: $\tau^2 = 0.05$; $\chi^2_8 = 16.09$; $P = .04$; $I^2 = 50\%$					
Tests for overall effect: z score = 0.53; $P = .59$					
Overall	470	5221	497	5316	0.97 (0.81-1.16)
Heterogeneity: $\tau^2 = 0.04$; $\chi^2_{21} = 29.75$; $P = .10$; $I^2 = 29\%$					
Tests for overall effect: z score = 0.29; $P = .77$					
Tests for subgroup differences: $\chi^2_1 = 0.34$; $P = .56$; $I^2 = 0\%$					

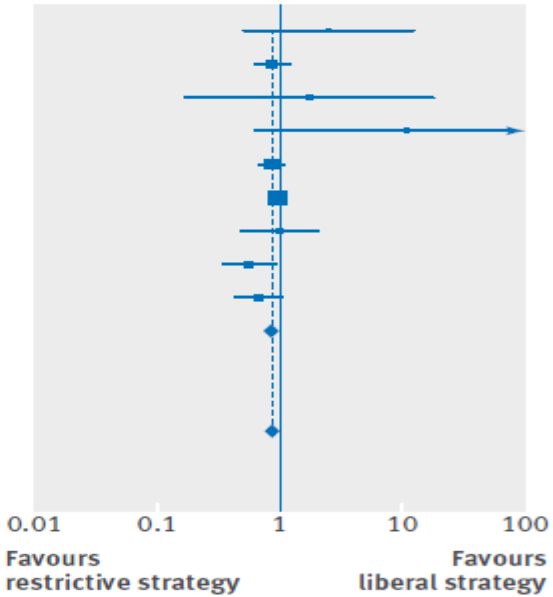


OR 0.97 (0.81-1.16)

The size of the data markers indicates the weight of the trial; RR, relative risk. Trials published after 2012 have been published since the prior AABB transfusion guidelines.

Relative risk 0.86 (low risk of bias trials) Estimated NNT 53

Study or subgroup	No of events/total: Restrictive transfusion	No of events/total: Liberal transfusion	Risk ratio M-H to random (95% CI)	Weight (%)	Risk ratio M-H to random (95% CI)
1.2.1 Low risk of bias					
Carson 1998[32]	5/42	2/42		1.0	2.50 (0.51 to 12.17)
Carson 2011[25]	66/1001	76/998		16.5	0.87 (0.63 to 1.19)
Cooper 2011[71]	2/24	1/21		0.5	1.75 (0.17 to 17.95)
Foss 2009[28]	5/60	0/60		0.3	11.00 (0.62 to 194.63)
Hébert 1999[4]	95/416	111/419		23.2	0.86 (0.68 to 1.09)
Holst 2014[9]	216/502	223/496		35.2	0.96 (0.83 to 1.10)
Lacroix 2007[5]	14/320	14/317		4.4	0.99 (0.48 to 2.04)
Villanueva 2013[6]	23/444	41/445		8.5	0.56 (0.34 to 0.92)
Walsh 2013[10]	19/51	27/49		10.4	0.68 (0.44 to 1.05)
Subtotal	445/2860	495/2847		100.0	0.86 (0.74 to 1.01)
Test for heterogeneity: τ^2=0.01, χ^2=10.96, df=8, P=0.20, I^2=27%					
Test for overall effect: z=1.79, P=0.07					
Total (95% CI)	445/2860	495/2847		100.0	0.86 (0.74 to 1.01)
Test for heterogeneity: τ^2=0.01, χ^2=10.96, df=8, P=0.20, I^2=27%					
Test for overall effect: z=1.79, P=0.07					
Test for subgroup differences: not applicable					



0.86 (0.74-1.01)

BMJ 2015;350:h1354

Reduces the risk of transfusion: 0.54 (0.47- 0.63; P<0.001)

And the number of units transfused (mean difference −1.43 unit, (−2.01 to −0.86; P<0.001)

Cost to put a single RBC unit into a patient US$741 in 2010

Holst L, et al. BMJ 2015;350:h1354

RBC - TRICC Study

- NEJM 1999; 340:409-17 - Hebert et al
  - n=838 non-bleeding, ICU patients, Hb <90 g/L
  - RCT - transfusion Hb <70 vs <100
  - Non-leukoreduced RBCs
  - Stratified by APACHE 2 score
  - Groups equal with respect to baseline characteristics
  - Average patient: 58 year old male, with 1-2 organ failure, mechanically vented, admitted to the ICU from the OR

Outcome - Mortality

Outcome	<70 g/L	<100 g/L	P value
30-day	18.7%	23.3%	P=0.11
Hospital	22.2%	28.1%	P=0.05

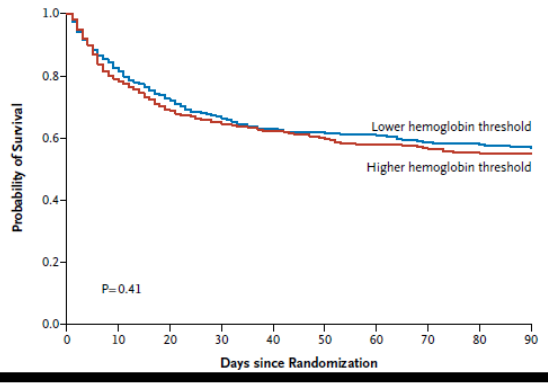
NNT = 17 patients to prevent one in-hospital death

Morbidity Outcomes in TRICC

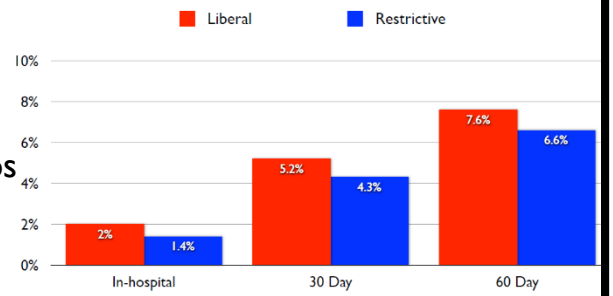
	Restrictive N (%)	Liberal N (%)	P Value
MI	3 (0.7)	12 (2.9)	0.02
Pulmonary Edema	22 (5.3)	45 (10.7)	0.01
ARDS	32 (7.7)	48 (11.4)	0.06

Key RBC Trials

TRISS
Holst
NEJM 2014
Septic Shock
n=998
70 vs 90 g/L
No subgroups



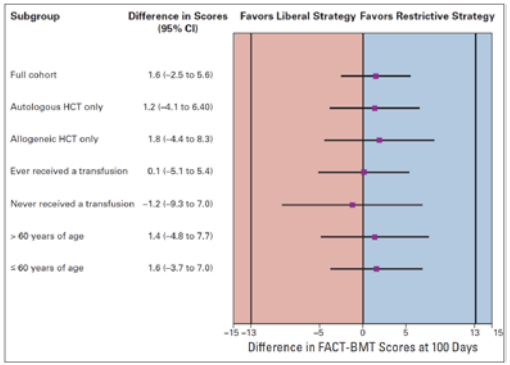
FOCUS
Carson
NEJM 2011
Fractured hips
Periop
n=2016
80 vs 100



TRICS III
Mazer
NEJM 2017
CVSx
n=5035
75 vs 95 g/L
No subgroups

Composite: 0.90 (0.76-1.07)
Death: 0.85 (0.62-1.16)
Stroke: 0.92 (0.61-1.38)
MI: 1.00 (0.79-1.27)
Kidney Failure: 0.84 (0.60-1.19)

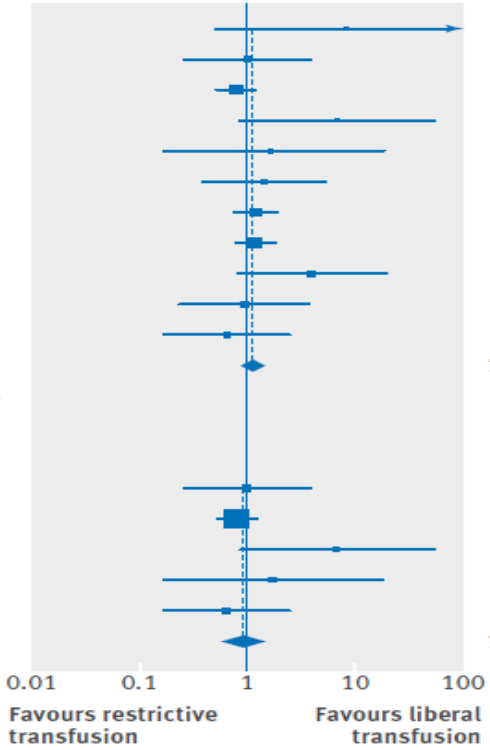
TRIST
Tay
JCO 2020
Hematology
n=300
70 vs 90



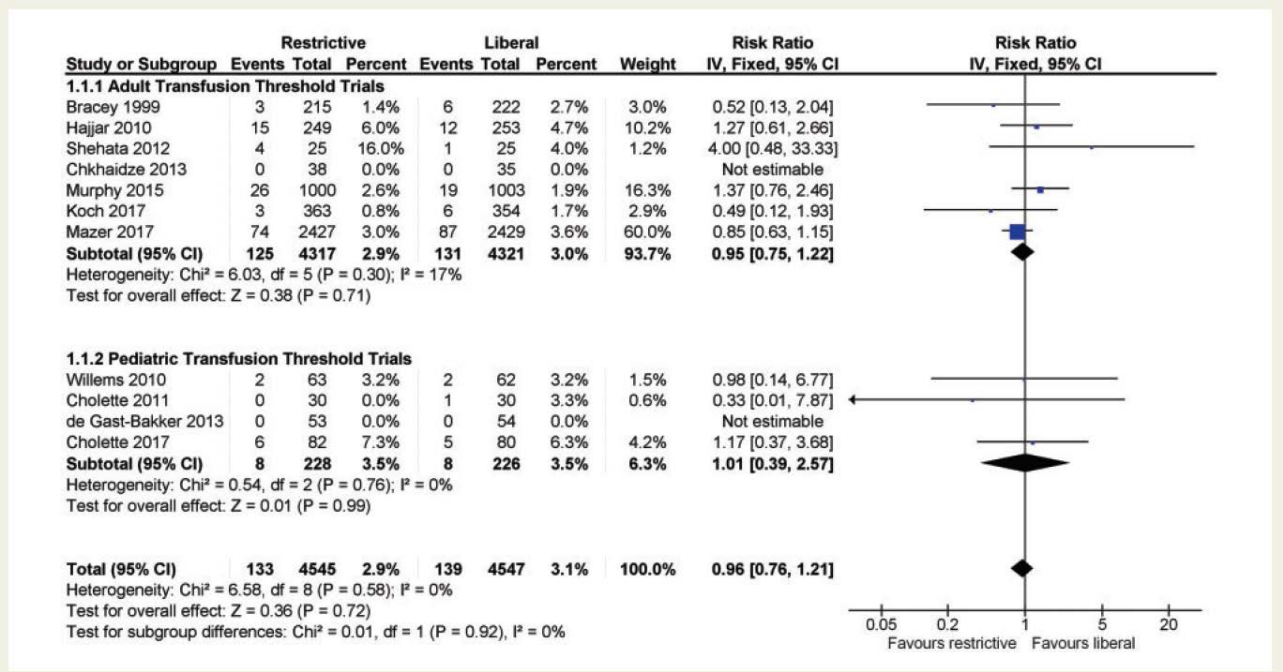
BMJ 2016;352:i1351

No benefit in CVD patients

Study	No of events/ total No of patients: Restrictive transfusion	Liberal transfusion	Risk ratio MH random effect (95% CI)	Weight (%)	Risk ratio MH random effect (95% CI)
All studies					
Almeida 2015	7/22	0/12		0.9	8.48 (0.53 to 136.76)
Bush 1997	4/49	4/50		3.8	1.02 (0.27 to 3.85)
Carson 2011	43/1008	52/995		27.7	0.82 (0.55 to 1.21)
Carson 2013	7/55	1/55		1.6	7.00 (0.89 to 55.01)
Cooper 2011	2/24	1/21		1.3	1.75 (0.17 to 17.95)
Gregersen 2015	6/34	3/25		4.0	1.47 (0.41 to 5.32)
Hebert 1999	29/111	31/146		23.9	1.23 (0.79 to 1.91)
Holst 2014	33/75	24/66		26.5	1.21 (0.80 to 1.82)
Jairath 2015*	6/49	2/67		2.8	4.10 (0.86 to 19.47)
Parker 2013	4/70	4/67		3.7	0.96 (0.25 to 3.67)
Walsh 2013	3/17	4/15		3.8	0.66 (0.18 to 1.50)
Total	144/1514	126/1519		100.0	1.15 (0.88 to 1.50)
Test for heterogeneity: τ^2=0.03, χ^2=11.58, df=10, P=0.31, I^2=14%					
Test for overall effect: z=1.04, P=0.30					
Studies randomised by CVD					
Bush 1997	4/49	4/50		3.8	1.02 (0.27 to 3.85)
Carson 2011	43/1008	52/995		27.7	0.82 (0.55 to 1.21)
Carson 2013	7/55	1/55		1.6	7.00 (0.89 to 55.01)
Cooper 2011	2/24	1/21		1.3	1.75 (0.17 to 17.95)
Walsh 2013	3/17	4/15		3.8	0.66 (0.18 to 1.50)
Total	59/1153	62/1136		100.0	0.96 (0.58 to 1.59)
Test for heterogeneity: τ^2=0.06, χ^2=4.67, df=4, P=0.32, I^2=14%					
Test for overall effect: z=0.17, P=0.87					



No benefit for cardiac surgery patients



Study or Subgroup	Restrictive Events	Restrictive Total	Restrictive Percent	Liberal Events	Liberal Total	Liberal Percent	Weight	Risk Ratio IV, Fixed, 95% CI
1.1.1 Adult Transfusion Threshold Trials								
Bracey 1999	3	215	1.4%	6	222	2.7%	3.0%	0.52 [0.13, 2.04]
Hajjar 2010	15	249	6.0%	12	253	4.7%	10.2%	1.27 [0.61, 2.66]
Shehata 2012	4	25	16.0%	1	25	4.0%	1.2%	4.00 [0.48, 33.33]
Chkhaidze 2013	0	38	0.0%	0	35	0.0%		Not estimable
Murphy 2015	26	1000	2.6%	19	1003	1.9%	16.3%	1.37 [0.76, 2.46]
Koch 2017	3	363	0.8%	6	354	1.7%	2.9%	0.49 [0.12, 1.93]
Mazer 2017	74	2427	3.0%	87	2429	3.6%	60.0%	0.85 [0.63, 1.15]
Subtotal (95% CI)	**125**	**4317**	**2.9%**	**131**	**4321**	**3.0%**	**93.7%**	**0.95 [0.75, 1.22]**
Heterogeneity: Chi² = 6.03, df = 5 (P = 0.30); I² = 17%								
Test for overall effect: Z = 0.38 (P = 0.71)								
1.1.2 Pediatric Transfusion Threshold Trials								
Willems 2010	2	63	3.2%	2	62	3.2%	1.5%	0.98 [0.14, 6.77]
Cholette 2011	0	30	0.0%	1	30	3.3%	0.6%	0.33 [0.01, 7.87]
de Gast-Bakker 2013	0	53	0.0%	0	54	0.0%		Not estimable
Cholette 2017	6	82	7.3%	5	80	6.3%	4.2%	1.17 [0.37, 3.68]
Subtotal (95% CI)	**8**	**228**	**3.5%**	**8**	**226**	**3.5%**	**6.3%**	**1.01 [0.39, 2.57]**
Heterogeneity: Chi² = 0.54, df = 2 (P = 0.76); I² = 0%								
Test for overall effect: Z = 0.01 (P = 0.99)								
Total (95% CI)	**133**	**4545**	**2.9%**	**139**	**4547**	**3.1%**	**100.0%**	**0.96 [0.76, 1.21]**
Heterogeneity: Chi² = 6.58, df = 8 (P = 0.58); I² = 0%								
Test for overall effect: Z = 0.36 (P = 0.72)								
Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.92), I² = 0%								

Figure 4 Mortality within 30 days of surgery in randomized controlled trials of adult and paediatric cardiac surgery patients. Fixed-effects meta-analysis.

OR 0.96 (0.76-1.21)

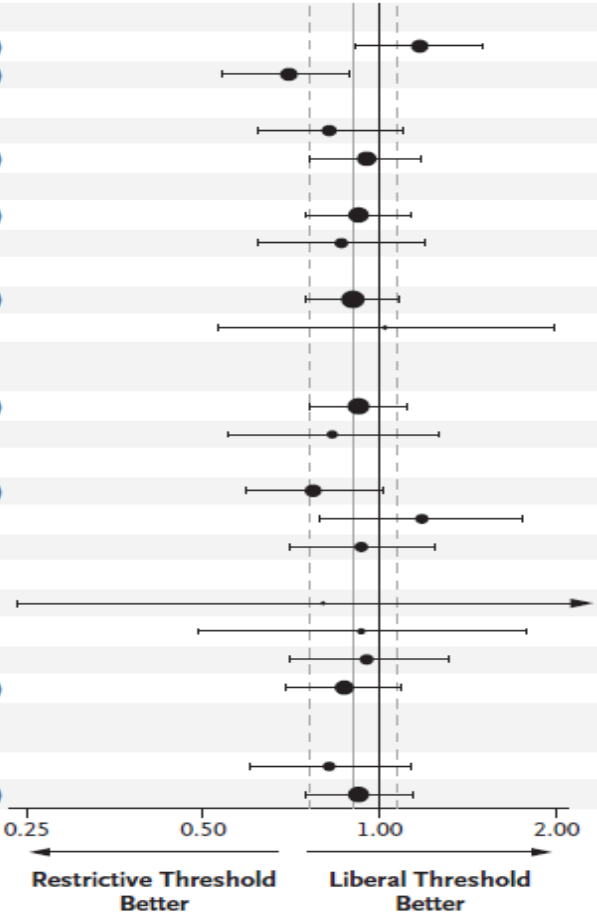
Shehata et al. Eur Heart J 2019; 1: 1081-1088

TRICS III

- 4860 patients undergoing cardiac surgery, mean age 72, 25% myocardial infarction in last 90 days, 55% some renal impairment
- RCT – 75 vs. 95 including during surgery
- Primary: death from any cause, myocardial infarction, stroke, or new onset renal failure with dialysis to 28 days
  - odds ratio, 0.90; 95% CI, 0.76 to 1.07

N Engl J Med 2017;377:2133-44.

Subgroup	No. of Patients	Restrictive Threshold	Liberal Threshold	Unadjusted Odds Ratio (95% CI)	P Value for Interaction
		no. of patients with event/total no. (%)			
Age					0.004
<75 yr	2426	152/1218 (12.5)	131/1208 (10.8)	1.17 (0.91–1.50)	
≥75 yr	2431	124/1210 (10.2)	172/1221 (14.1)	0.70 (0.54–0.89)	
Sex					0.45
Female	1719	99/876 (11.3)	113/843 (13.4)	0.82 (0.62–1.10)	
Male	3138	177/1552 (11.4)	190/1586 (12.0)	0.95 (0.76–1.18)	
Diabetes					0.75
No	3526	200/1783 (11.2)	211/1743 (12.1)	0.92 (0.75–1.13)	
Yes	1331	76/645 (11.8)	92/686 (13.4)	0.86 (0.62–1.19)	
Creatinine level					0.71
≤2.26 mg/dl	4685	253/2348 (10.8)	277/2337 (11.9)	0.90 (0.75–1.08)	
>2.26 mg/dl	172	23/80 (28.7)	26/92 (28.3)	1.02 (0.53–1.99)	
Chronic pulmonary disease					0.67
No	4057	229/2023 (11.3)	249/2034 (12.2)	0.92 (0.76–1.11)	
Yes	800	47/405 (11.6)	54/395 (13.7)	0.83 (0.55–1.26)	
Surgery category					0.22
Non-CABG	2247	111/1138 (9.8)	136/1109 (12.3)	0.77 (0.59–1.01)	
CABG only	1266	57/621 (9.2)	51/645 (7.9)	1.18 (0.79–1.75)	
CABG+ other	1344	108/669 (16.1)	116/675 (17.2)	0.93 (0.70–1.24)	
Left ventricular function					0.78
Very poor	84	6/46 (13.0)	6/38 (15.8)	0.80 (0.24–2.72)	
Poor	322	21/166 (12.7)	21/156 (13.5)	0.93 (0.49–1.78)	
Moderate	1441	88/731 (12.0)	89/710 (12.5)	0.95 (0.70–1.31)	
Good	3010	161/1485 (10.8)	187/1525 (12.3)	0.87 (0.69–1.09)	
Preoperative hemoglobin concentration					0.54
<12.0 g/dl	1149	84/593 (14.2)	93/556 (16.7)	0.82 (0.60–1.13)	
≥12.0 g/dl	3708	192/1835 (10.5)	210/1873 (11.2)	0.92 (0.75–1.14)	



Composite: 0.90 (0.76-1.07)
Death: 0.85 (0.62-1.16)

N Engl J Med 2017;377:2133-44.

REALITY Trial – RCT 80 vs. 100 g/L in patients with acute myocardial infarction

Table 3. Primary and Secondary Outcomes at 30 Days Among the As-Randomized Population in a Study of the Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Patients With Acute Myocardial Infarction and Anemia

Outcome	No. (%)		Difference (95% CI), %	Relative risk (1-sided 97.5% CI)
	Restrictive	Liberal		
Primary (major adverse cardiovascular events), No./total No. (%) [95% CI][a]				
As-treated population	36/327 (11.0) [7.5 to 14.6]	45/322 (14.0) [10.0 to 17.9]	−3.0 (−8.4 to 2.4)	0.79 (0.00 to 1.19)
As-randomized population	38/342 (11.1) [7.6 to 14.6]	46/324 (14.2) [10.2 to 18.2]	−3.1 (−8.4 to 2.3)	0.78 (0.00 to 1.17)

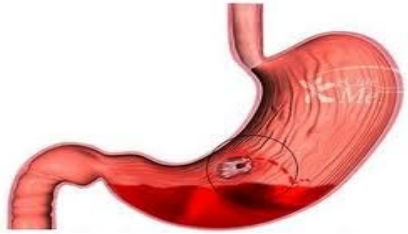
JAMA. 2021;325(6):552-560. doi:10.1001/jama.2021.0135

ACP Clinical Practice recommendations

- Patients: Adults with CHF/CHD and anemia
- RBC: No benefit to a liberal transfusion strategy
- Recommendation: ACP recommends a restrictive transfusion strategy (**70-80 g/L**) for patients with CHD

Ann Intern Med 2013; 159: 770-79.

Acute UGI Bleeding



921 pts with severe UGIB

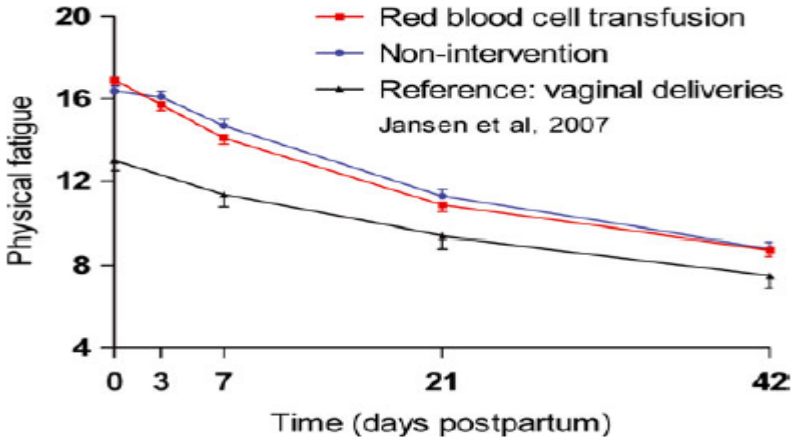
- **Restrictive Hb < 70 g/L**
- **Liberal Hb < 90 g/L**

6 week survival	95%	91%	P=0.02
Further bleeding	10%	16%	P=0.05
Adverse events	40%	48%	P=0.02
RBC transfusion	1.5 units	3.7 units	P<0.001
No RBC transfusion	51%	15%	P<0.001

Villanueva et al. NEJM Jan 2013;368:11-21

PPH – WOMB Trial

- 37 Dutch hospitals, 521 women randomized
- PPH with >1000 ml, Hb drop of 19+ points, and hemoglobin between 48-79 g/L, no severe symptoms of anemia (dyspnea, syncope, HR>100)
- Randomized to transfusion or no transfusion



BJOG 2014;121:1005–1014.

Table 2. Blood loss, haemoglobin concentration, and RBC transfusion

Variable	Transfusion (*n* = 258)	Non-intervention (*n* = 261)	*P*
RBC transfusion			
Units per woman	2 (2–2)	0 (0–0)	<0.001
Total units*	517	88	<0.001
Hb concentration after transfusion, g/dl)**	9.0 (8.5–9.6)	8.9 (8.2–9.7)	0.56
Hb concentration at discharge (g/dl)***	9.0 (8.5–9.5)	7.4 (6.8–7.7)	<0.001
Hb concentration at 6 weeks (g/dl)****	12.1 (11.3–12.6)	11.9 (10.9–12.6)	0.18

48

AABB RBC Guideline 2016

- Transfusion is not indicated until the hemoglobin is 70 g/L for hospitalized, hemodynamically stable patients (including ICU patients) – strong recommendation, moderate quality evidence
- For orthopedic and cardiac surgery and those with pre-existing cardiovascular disease, the AABB recommends 80 g/L (strong recommendation, moderate quality evidence)
  - 80 g/L likely comparable to 70 g/L but RCT evidence not available for all groups
- Acute coronary syndrome – no recommendation

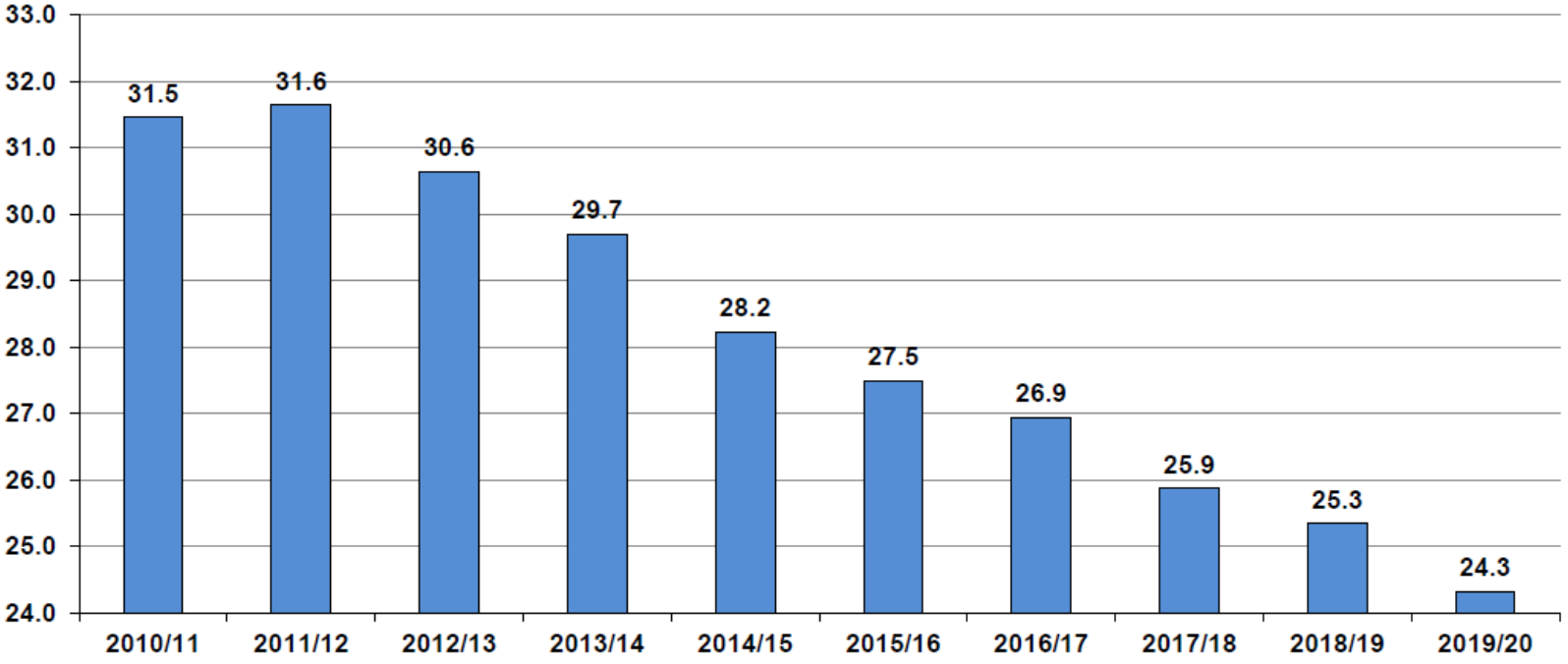
JAMA. 2016;316(19):2025-2035. doi:10.1001/jama.2016.9185
Published online October 12, 2016.

2018 Frankfurt Guidelines

- Newer but same as AABB plus:
  - The panel recommended a restrictive RBC transfusion threshold (hemoglobin concentration <75 g/L) in patients undergoing cardiovascular surgery
  - The panel recommended a restrictive transfusion threshold (hemoglobin concentration 70-80 g/dL) in hemodynamically stable patients with acute gastrointestinal bleeding

Mueller et al. JAMA. 2019;321(10):983-997

Right direction: RBC Units per 1,000 Population



Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Comparison to the Rest of the World

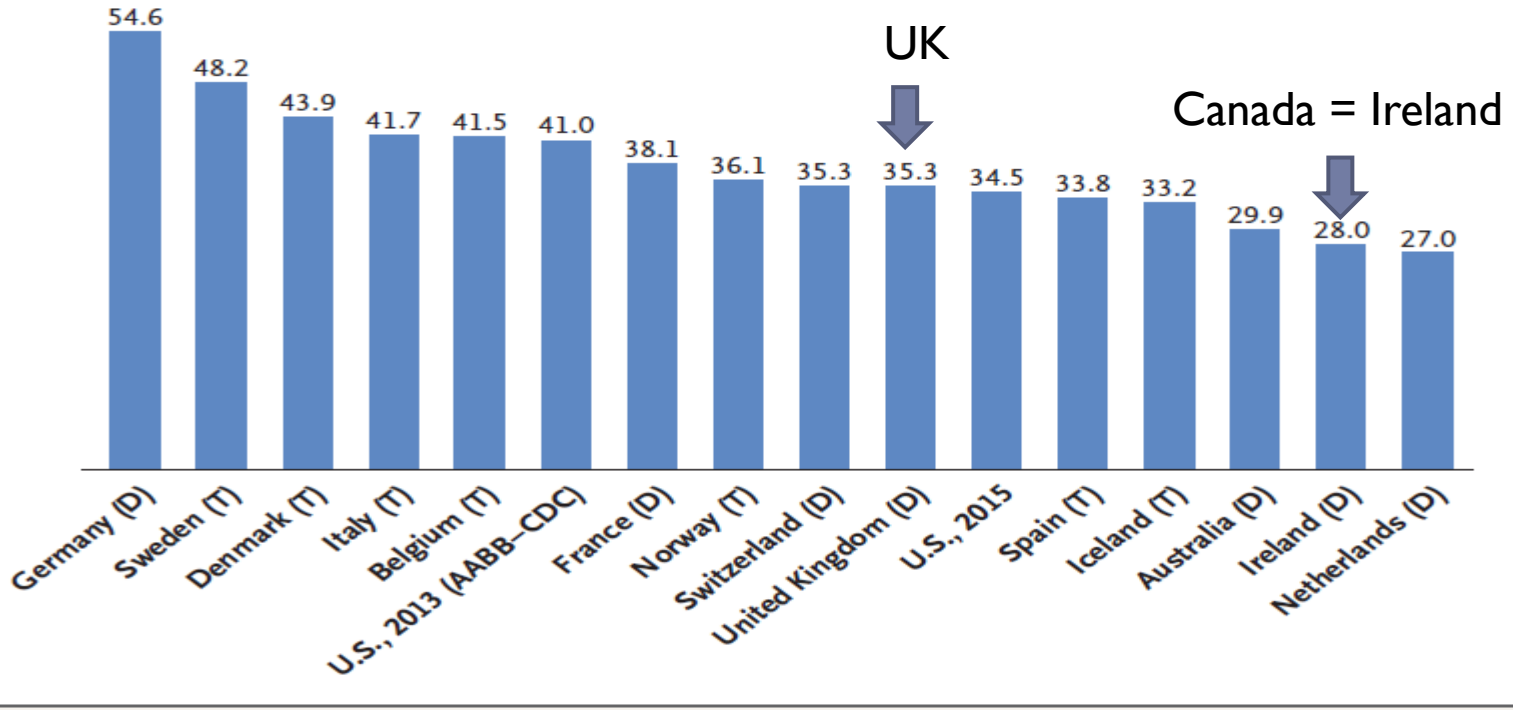
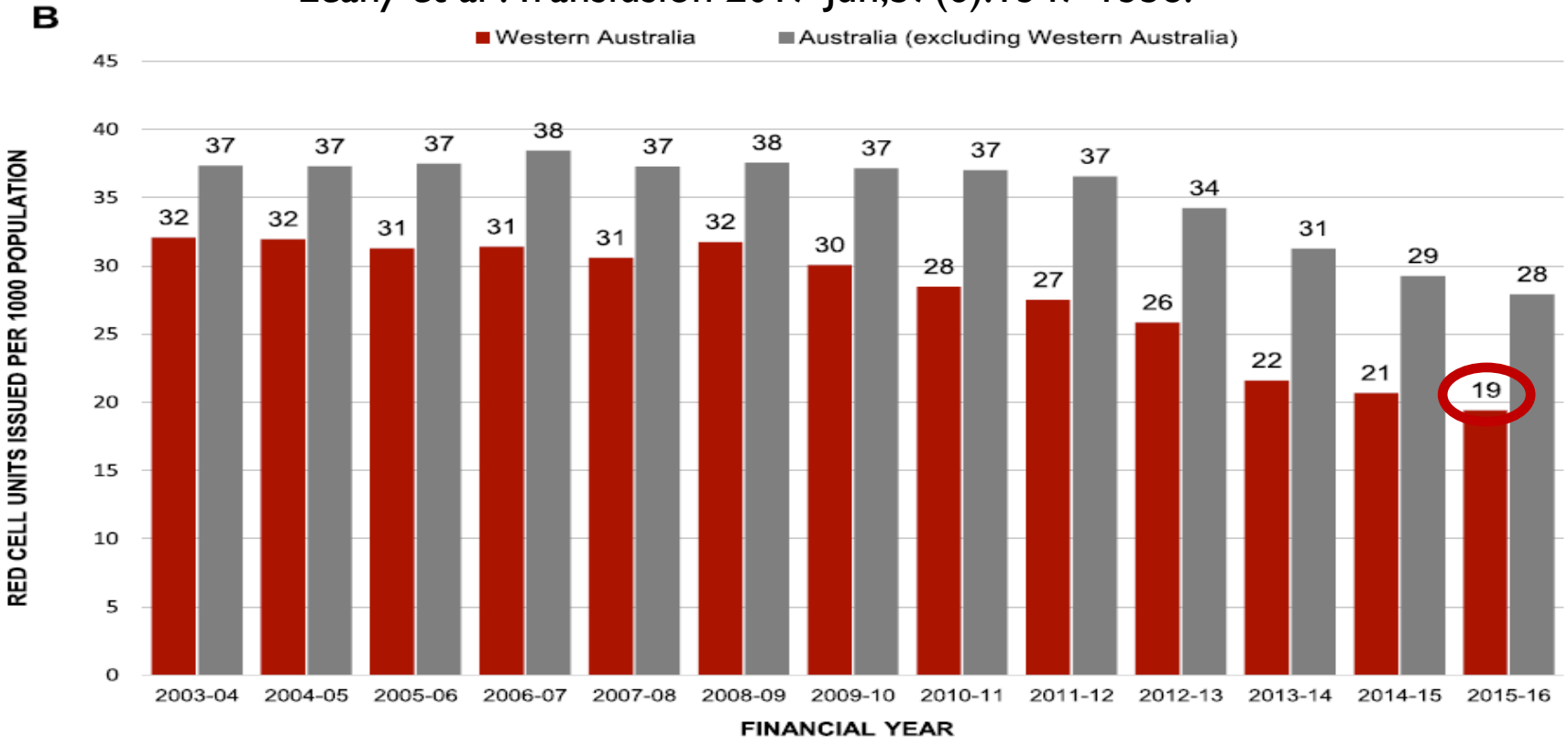


Figure 3. Transfusion Rates in the United States in 2013 and 2015, as Compared with Rates in Other Developed Countries.

N Engl J Med 2017;377:1261-72.

What patient blood management adds to restrictive transfusion thresholds

Leahy et al . Transfusion 2017 Jun;57(6):1347-1358.



Reasonable approach for inpatients

Remember not to transfuse for pallor/fatigue!

Patient scenario	Hemoglobin threshold	Transfusion approach
Young patient with severe iron or B12 deficiency anemia with only fatigue and pallor	Any	Iv iron (or B12 im/po)
Young patient with reversible asymptomatic anemia (eg. Postpartum, recovering young trauma)	<50 g/L	1 unit
Average patient without symptoms or cardiac history (eg. ICU, CVICU, hem-onc)	<70 g/L	1 unit
Cardiac history without symptoms	<70-80 g/L	1 unit
Hemodynamic symptoms (tachycardia, pre-syncope, etc)	<90 g/L	1 unit
Myocardial infarction with only fatigue and pallor	<80 g/L	1 unit GO SLOW
Slow bleeding and asymptomatic anemia	<70 g/L	1-2 units
Rapid hemorrhage (eg. Stabbing, gunshot, varices)	Keep 60-110 g/L	As many as you need! Don't forget to use the term uncrossmatched!

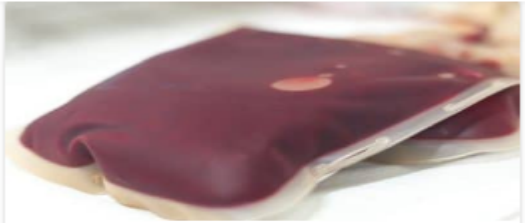
Summary

- Use these trials to help set your 'general' transfusion trigger where you might **consider** a transfusion
- Don't be overly prescriptive – just because the hemoglobin is 69 g/L you have to transfuse…or 71 g/L and you hold off
- Look at your patient – Are they symptomatic? Adjust the trigger to your patient's co-morbidities
- Unless rapid bleeding 1 unit at a time (inpatients)
- Write a rate
- Anticipate and prevent TACO

5 Things I hope you will do in 2021

1. Give iron deficient patients iron instead of blood unless clear hemodynamic instability
2. Make extra efforts for young women to prevent transfusion and alloimmunization risk
3. Adopt a restrictive transfusion approach for most patients
4. Transfuse one at a time (even in the operating room) unless brisk bleeding – check hemoglobin after every unit
5. Think about the other patient (the donor) when you transfuse – we have a duty of care to the other patient

BloodBankGuy



023: RBC Transfusion Guidelines with Jeff Carson

Whither RBCs? There's no one better than lead author Dr. Jeff Carson to discuss the 2016 AABB RBC transfusion threshold recommendations!

035: Why Give Platelets? with Rick Kaufman

Platelets are tiny, but they can be a big issue! Dr. Rick Kaufman magnifies what the evidence shows about platelet transfusion.

Listen to This Episode!

016: Plasma Transfusion with Jeannie Callum

As many as 50% of plasma transfusions are unnecessary or inappropriate! You need to know why, and Dr. Jeannie Callum explains it SO well!