RBCs & Platelet Update

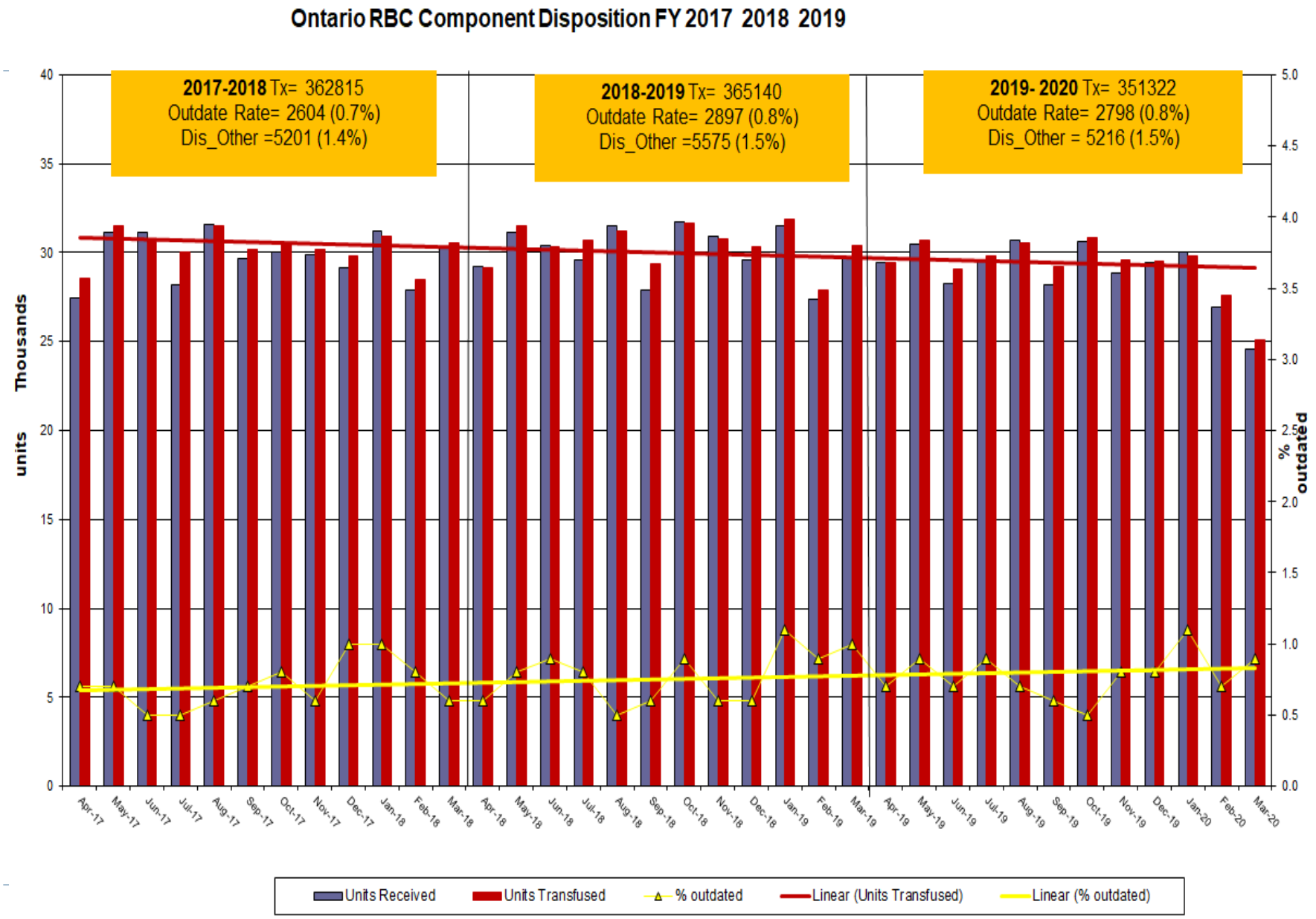
Are you up to date with the published guidelines?

Jan 2021

Disclosure

- Funding from TEM International, and CSL Behring for a step-wedged cluster RCT comparing ROTEM vs. conventional lab testing for cardiac surgery bleeding (participating site)
- Funding from Octapharma for a pragmatic RCT of cryoprecipitate vs. fibrinogen for post cardiac surgery bleeding
- Funding from the Defense Research and Development Canada for a fibrinogen concentrate RCT in trauma
- Funding from Canadian Blood Services to validate platelet bags for MHP protocols
- Funding from Canadian Blood Services for an RCT of lasix vs. no lasix before RBC transfusions – TACO-BEL trials (x4)
- Funding from Canadian Blood Services for the START trial

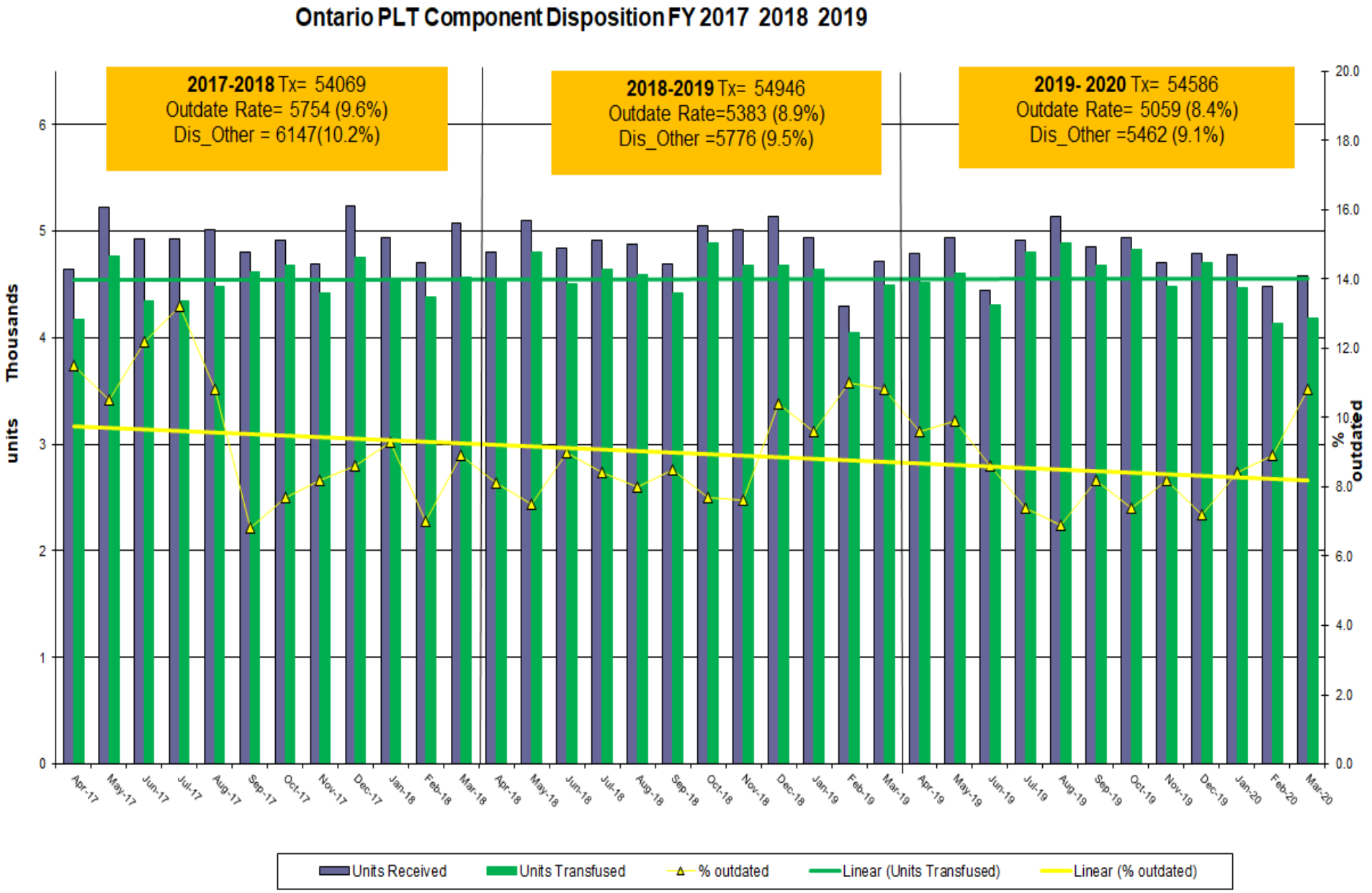
Provincial Red Cell Utilization



O Negative Blood Use

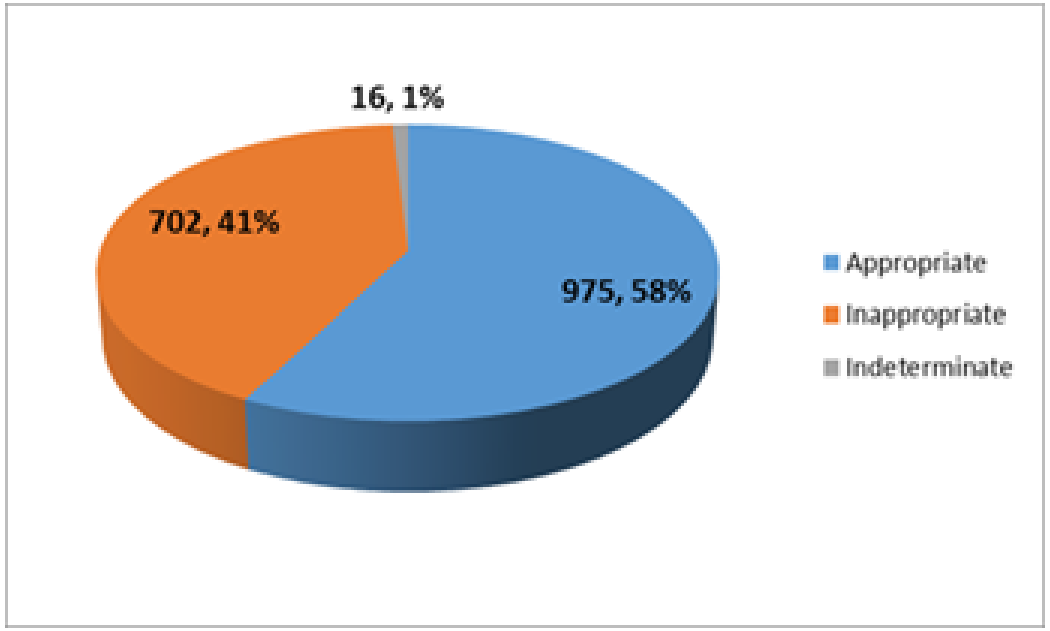
RBCs Issued 2019/20			
	All Units	O Neg	Percentage
National	708 108	86 329	12.2 %
Ontario	352 514	39 796	11.3 %

Provincial Platelet Utilization



Platelet Audit Results

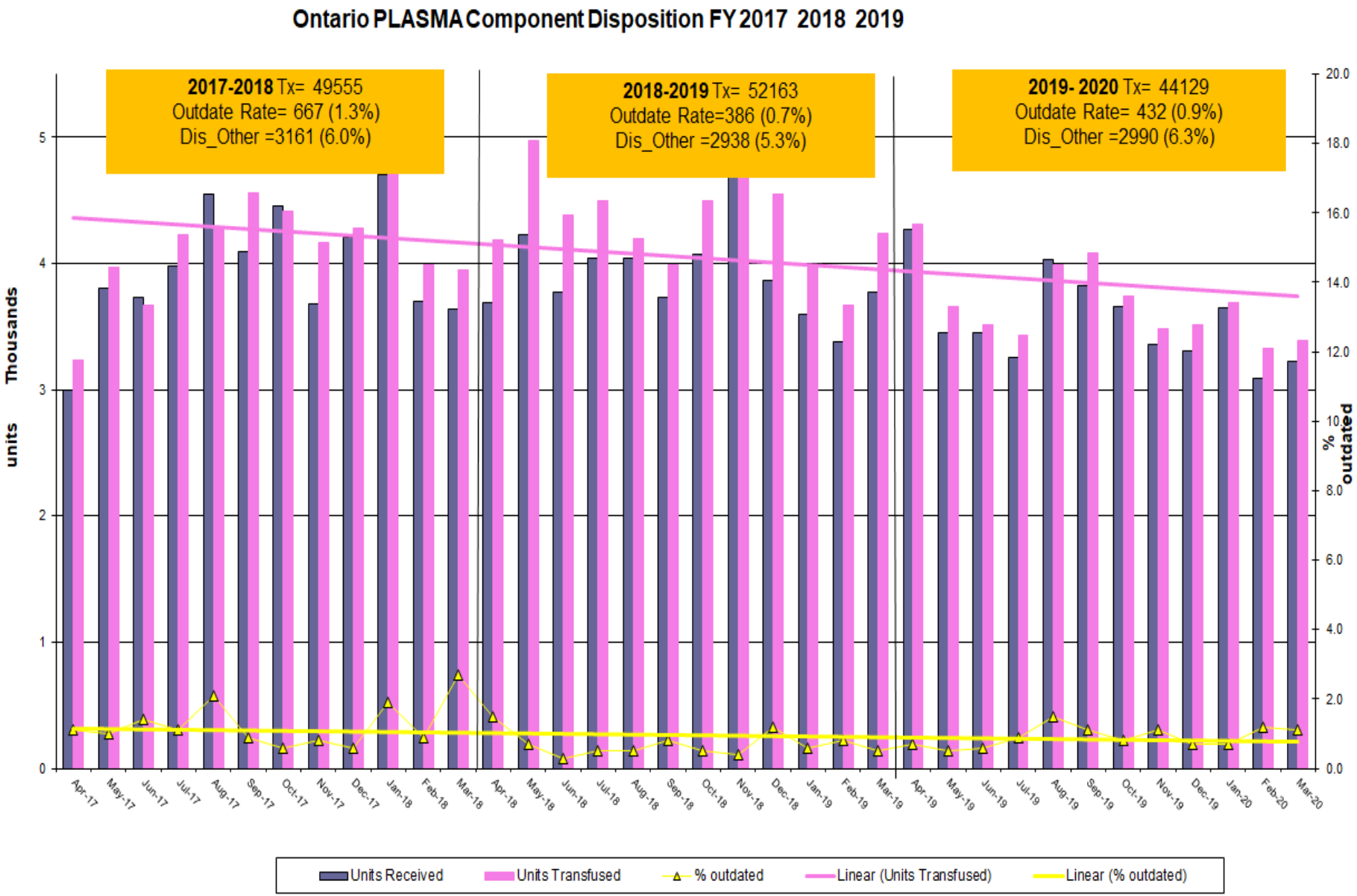
- 1693 adult platelet orders



Platelet Audit Results

Highest 3 Inappropriate Categories for Adult Orders	# (%) of Inappropriate
Prophylaxis for spontaneous bleeding Non-immune thrombocytopenia • Hypoproliferative thrombocytopenia due to hematologic malignancies, hematopoietic cell transplant or cytotoxic chemotherapy, sepsis or medication induced • Platelet count >10	371 (53)
Therapeutic • Major elective non-neuraxial surgery or procedures associated with major blood loss > 500 ml (up to 48 hours post-op) • Platelet count ≥50	72 (10)
Therapeutic • Non - CNS bleeding WHO grade 2 • Platelet count ≥30	62 (9)

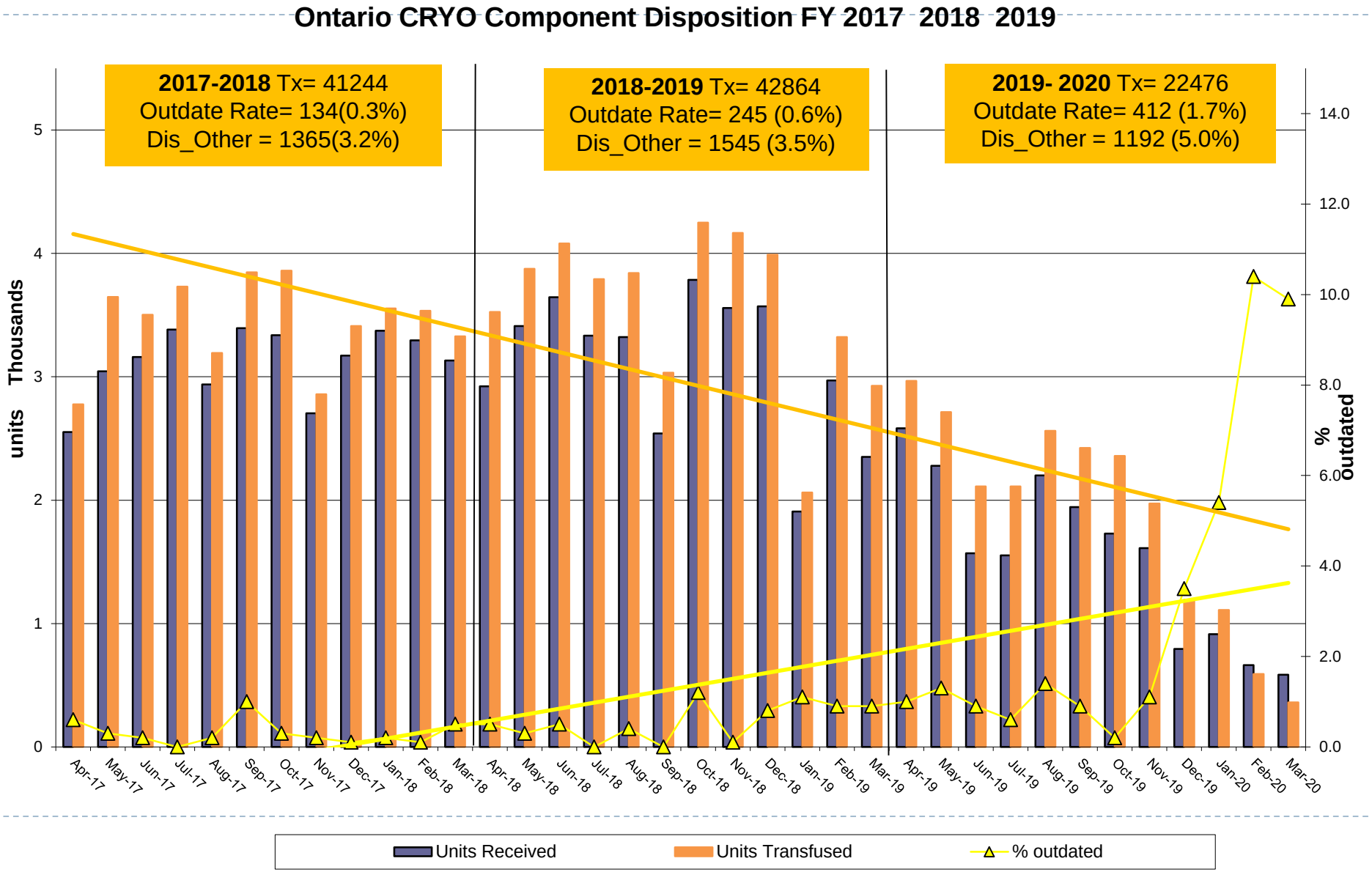
Provincial Plasma Utilization



AB Plasma Issued Statistics

AB Plasma Issued 2019/20			
	All ABO Issued	AB Issued	%AB
National	105,302	16,422	15.6%
Ontario	53,532	9,020	16.8%

Provincial Cryoprecipitate Utilization



Outline

- Why wouldn't you want to transfuse RBCs and PLTs to a patient?
  - There is a down side!
- When should you give RBCs?
  - Multiple randomized trials and meta-analyses to guide your decisions
- When should you give PLTs?
  - Multiple randomized trials and large cohort studies to guide your decisions

Both RBC and PLT transfusion decisions are now based on science, not the art of medicine.

Case

- 69 year old female, G5P5 with metastatic cholangiocarcinoma admitted with ischemic stroke, renal and splenic infarcts thought to be secondary to cancer-related hypercoagulable state
- Hb 74 g/L, asymptomatic, anti-Fya
- Prior to transfusion in no respiratory distress (on 1L/NP) with sat of 94%
- 1 unit over 2 hours ordered, no pre-transfusion furosemide
- At 15 minute and approx. 15 mL infused she developed hypotensive shock, fever, hypoxia, and bilateral infiltrates
- Within 12 hours she expired due to progressive respiratory failure

Case

- Investigation:
  - Donor 62 year old female with anti-HLA-DQA1, DQ7, DQ8, and DQ9 antibodies (HLA class II not available on patient) and B1-pack red cell (<2 mL plasma)
  - Recipient:
    - anti-HLA-A2, B35, 44, Bw4 (recipient positive for all antigens)
    - anti-HPA-5b
    - Anti-HNA-1a, 5a (recipient positive for both antigens)
- Conclusion: Fatal Transfusion-related Acute Lung Injury (TRALI)

The risks of RBCs & PLTs

Why you should always have some reluctance to order

Risks of RBCs

- **Transfusion associated circulatory overload**
  - ***Probably really common – 1-6% of adults***
- Transfusion-related acute lung injury
  - Rate 1 in 10,000
- Acute and delayed hemolytic transfusion reactions
  - ABO-immune hemolysis (by mistake)
  - RBC alloantibodies 1 in 13 (HDFN risk for girls and young women)
  - Delayed hemolytic transfusion reactions 1 in 7000
- More bleeding (from GI bleeding trials)
- HLA alloimmunization and risk of transplant ineligibility
- Iron loading

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

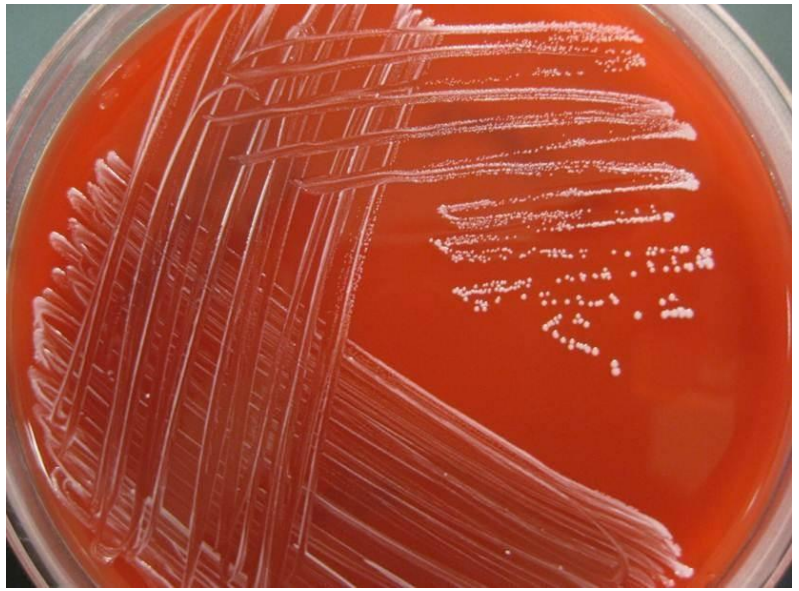
bloody easy 4, Ontario Transfusion Handbook, 2016.

What about PLT transfusion risks?

- Febrile non-hemolytic transfusion reaction (1 in 20)
- Urticarial reaction (1 in 100)
- **Bacterial sepsis (1 in 10,000)**
- **Acute hemolytic reaction** (group O platelet to a non-O recipient; aka "Dangerous Group O Donor")

Bacterial Sepsis from Platelets

- Blood agar plate vs. hematologist
- Agar 20, hematologists *zero*
- 1 in 2,600 infected (n=20)
- 1 in 10,000 symptomatic sepsis (n=5)
  - All hematology patients
  - 4 of 5 were outpatients
  - Onset 9-24 hours post-transfusion
  - All moderate to life-threatening
  - 1 died
  - None recognized as BaCon



Science not the "Art of Medicine"

Pertinent RBC Trials
33 RCTs with 18,083 patients

restrictive (70-75-80) vs. liberal (90-95-100)

Pre-TRICC

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

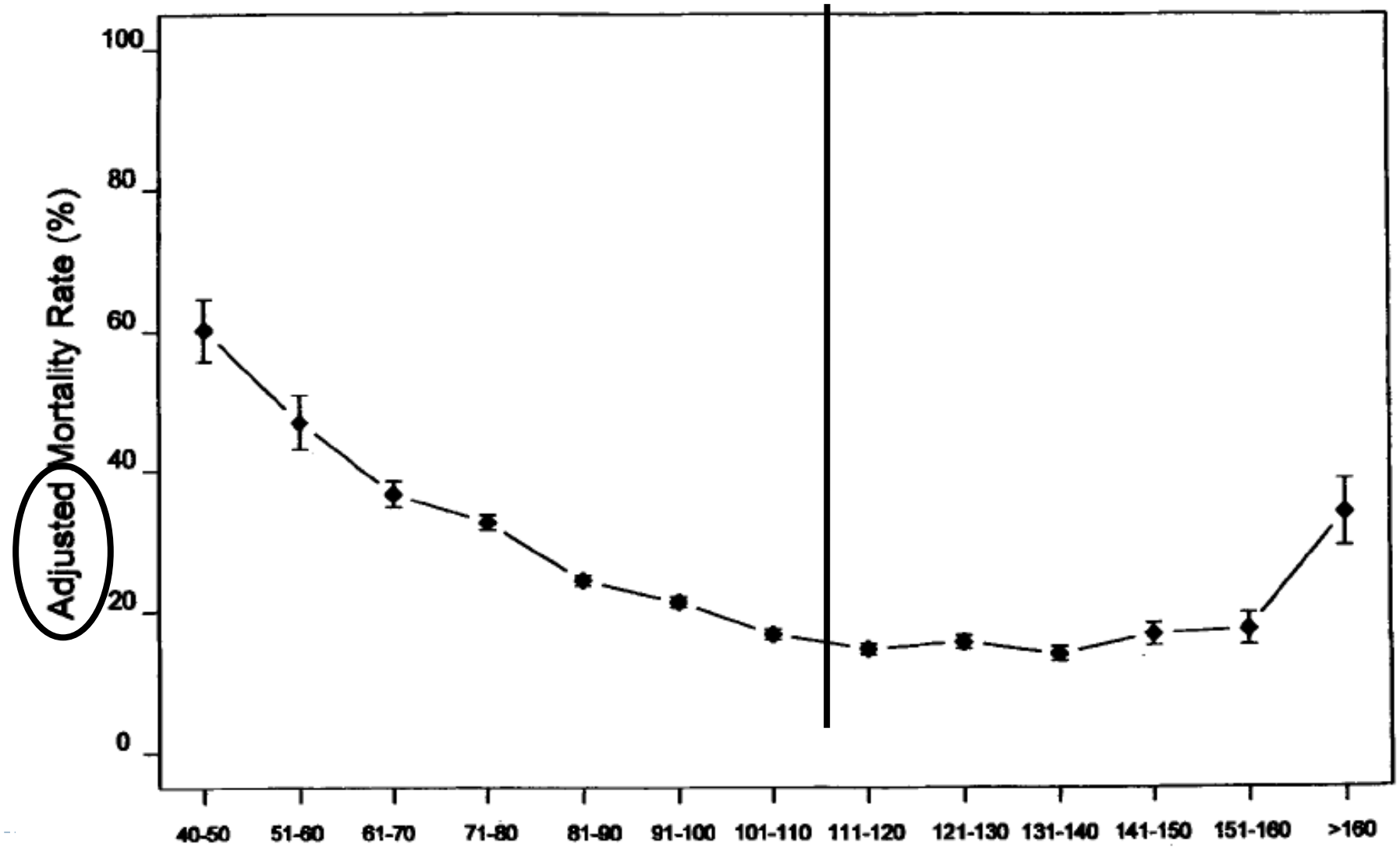
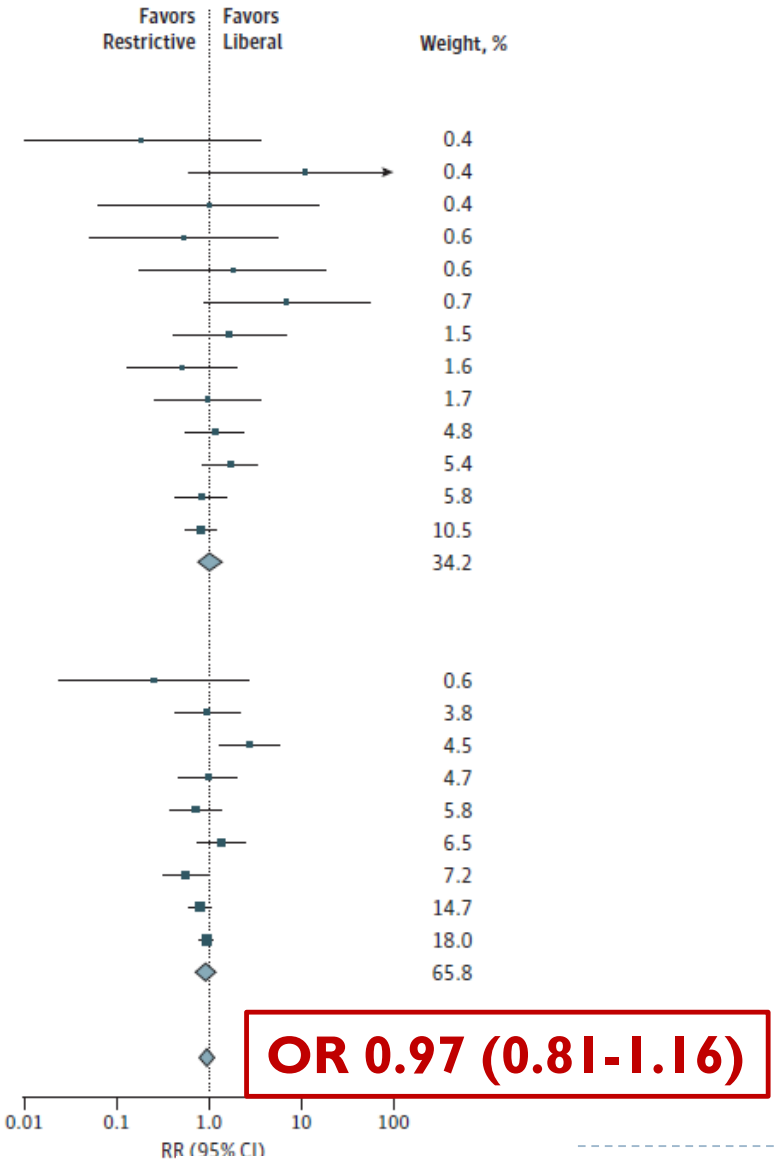


Figure 1. Comparison of 30-Day Mortality Using Restrictive vs Liberal Hemoglobin Transfusion Thresholds in Randomized Clinical Trials

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% CI)	Weight, %
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)	0.4
Foss et al,[63] 2009	5	60	0	60	11.00 (0.62-194.63)	0.4
Carson et al,[58] 1998	1	42	1	42	1.00 (0.06-15.47)	0.4
Webert et al,[86] 2008	1	29	2	31	0.53 (0.05-5.58)	0.6
Cooper et al,[61] 2011	2	23	1	21	1.83 (0.18-18.70)	0.6
Carson et al,[56] 2013	7	55	1	55	7.00 (0.89-55.01)	0.7
Parker,[78] 2013	5	100	3	100	1.67 (0.41-6.79)	1.5
Bracey et al,[54] 1999	3	215	6	222	0.52 (0.13-2.04)	1.6
Bush et al,[55] 1997	4	50	4	49	0.98 (0.26-3.70)	1.7
Hajjar et al,[68] 2010	15	249	13	253	1.17 (0.57-2.41)	4.8
Gregersen et al,[64] 2015	21	144	12	140	1.70 (0.87-3.32)	5.4
Jairath et al,[72] 2015	14	257	25	382	0.83 (0.44-1.57)	5.8
Carson et al,[60] 2011	43	1009	52	1007	0.83 (0.56-1.22)	10.5
Subtotal	121	2321	122	2451	1.05 (0.78-1.40)	34.2
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)	0.6
Hébert et al,[70] 1995	8	33	9	36	0.97 (0.42-2.22)	3.8
de Almeida et al,[79] 2015	23	101	8	97	2.76 (1.30-5.87)	4.5
Lacroix et al,[74] 2007	14	320	14	317	0.99 (0.48-2.04)	4.7
Walsh et al,[85] 2013	12	51	16	49	0.72 (0.38-1.36)	5.8
Murphy et al,[76] 2015	26	1000	19	1003	1.37 (0.76-2.46)	6.5
Villanueva et al,[84] 2013	19	416	34	417	0.56 (0.32-0.97)	7.2
Hébert et al,[69] 1999	78	418	98	420	0.80 (0.61-1.04)	14.7
Holst et al,[71] 2014	168	502	175	496	0.95 (0.80-1.13)	18.0
Subtotal	349	2900	375	2865	0.94 (0.74-1.19)	65.8
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 si

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

Reduces the risk of transfusion: 0.54 (95% CI: 0.47 to 0.63; P<0.001; I2=95%)

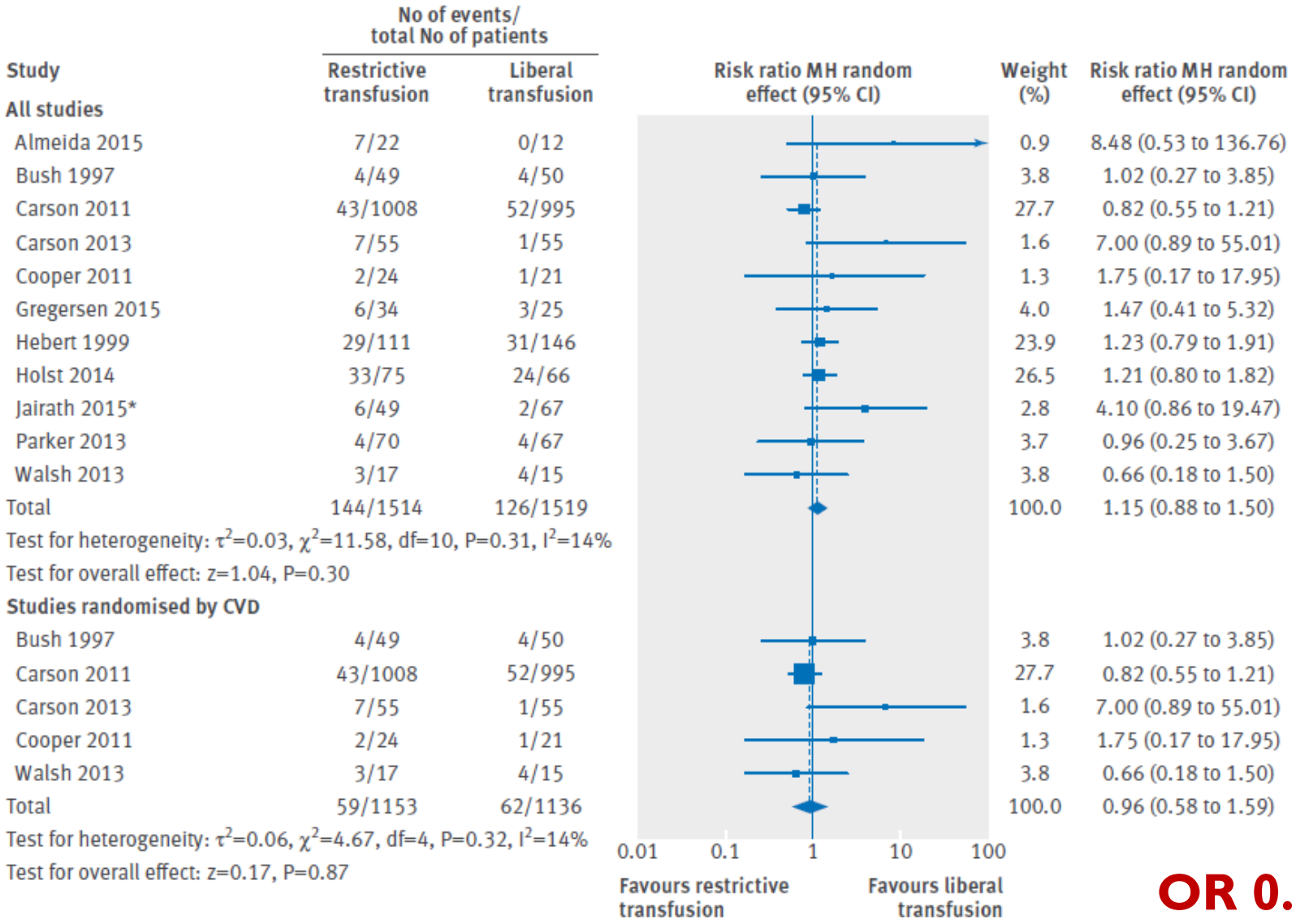
And the number of units transfused (mean difference −1.43 unit, 95% CI −2.01 to −0.86; P<0.001)

Cost to put a single RBC unit into a patient $1000

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

BMJ 2016;352:i1351

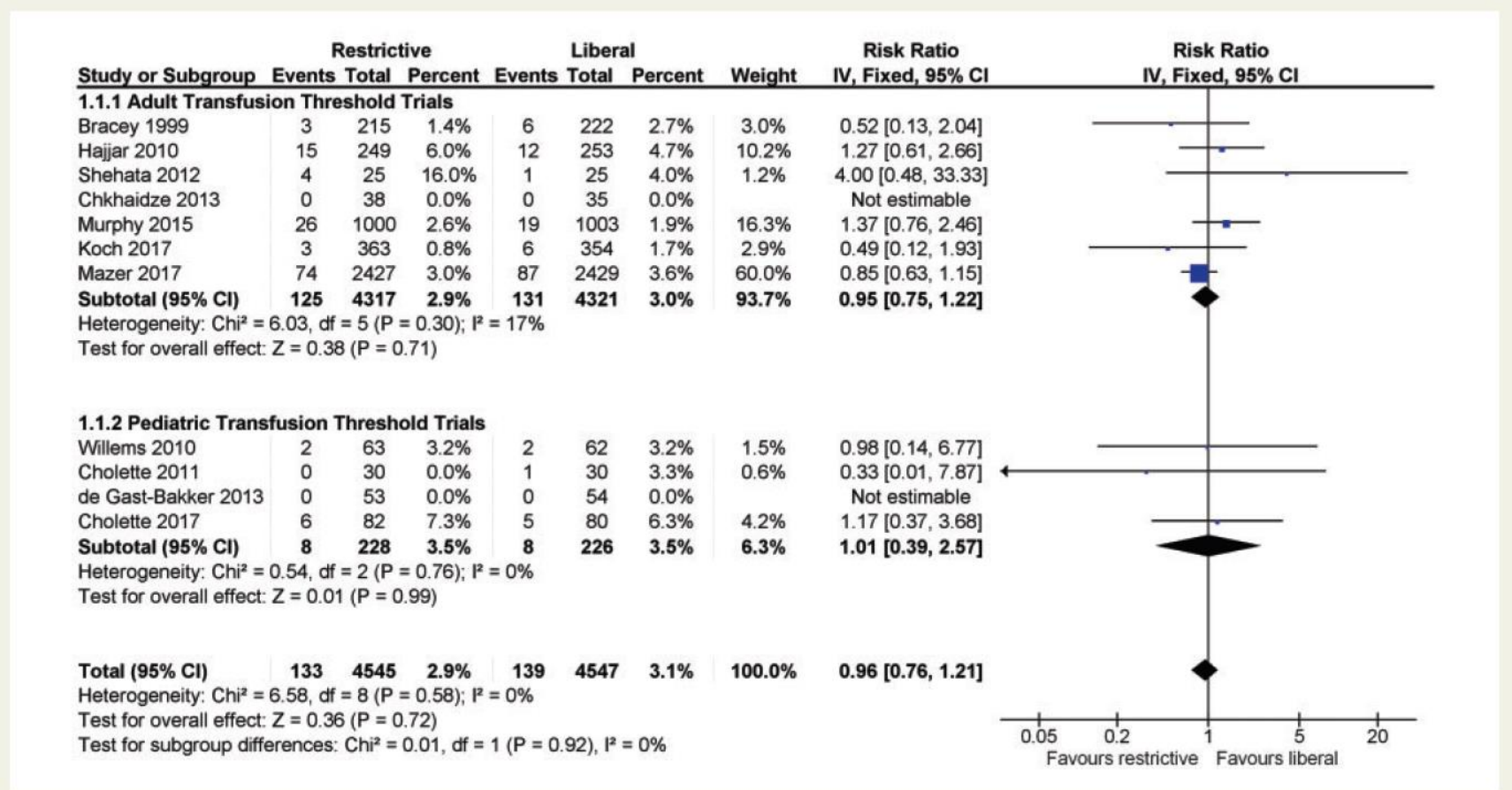
No benefit in CVD patients



Study	No of events/ total No of patients: Restrictive transfusion	Liberal transfusion	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				

OR 0.96 (0.58-1.59)

No benefit for cardiac surgery patients



Study or Subgroup	Restrictive Events	Total	Percent	Liberal Events	Total	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)

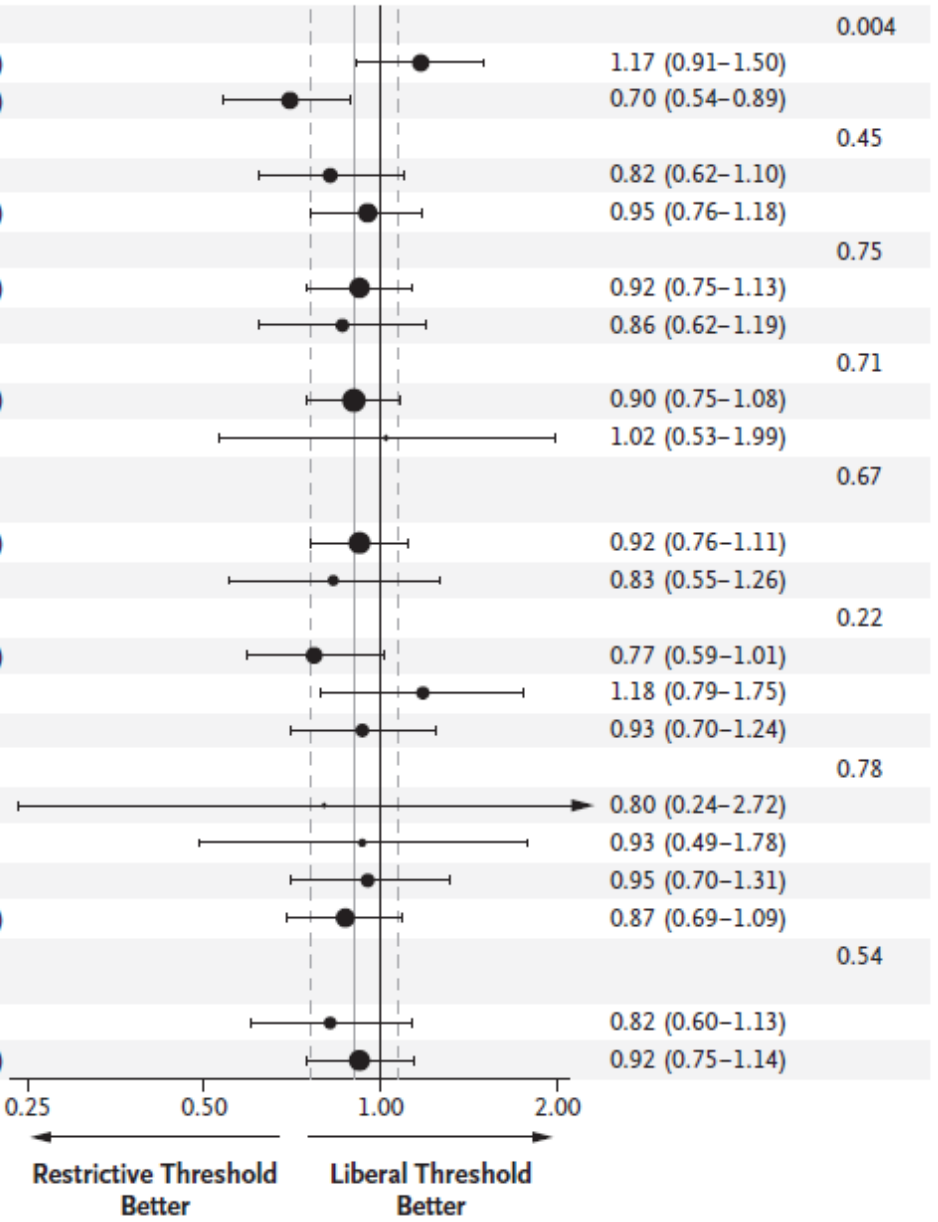
Shehata et al. Eur Heart J 2019; 1: 1081-1088

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
- Note: MINT Trial underway across USA and Canada – please try to enroll patients

Ann Intern Med 2013; 159: 770-79.

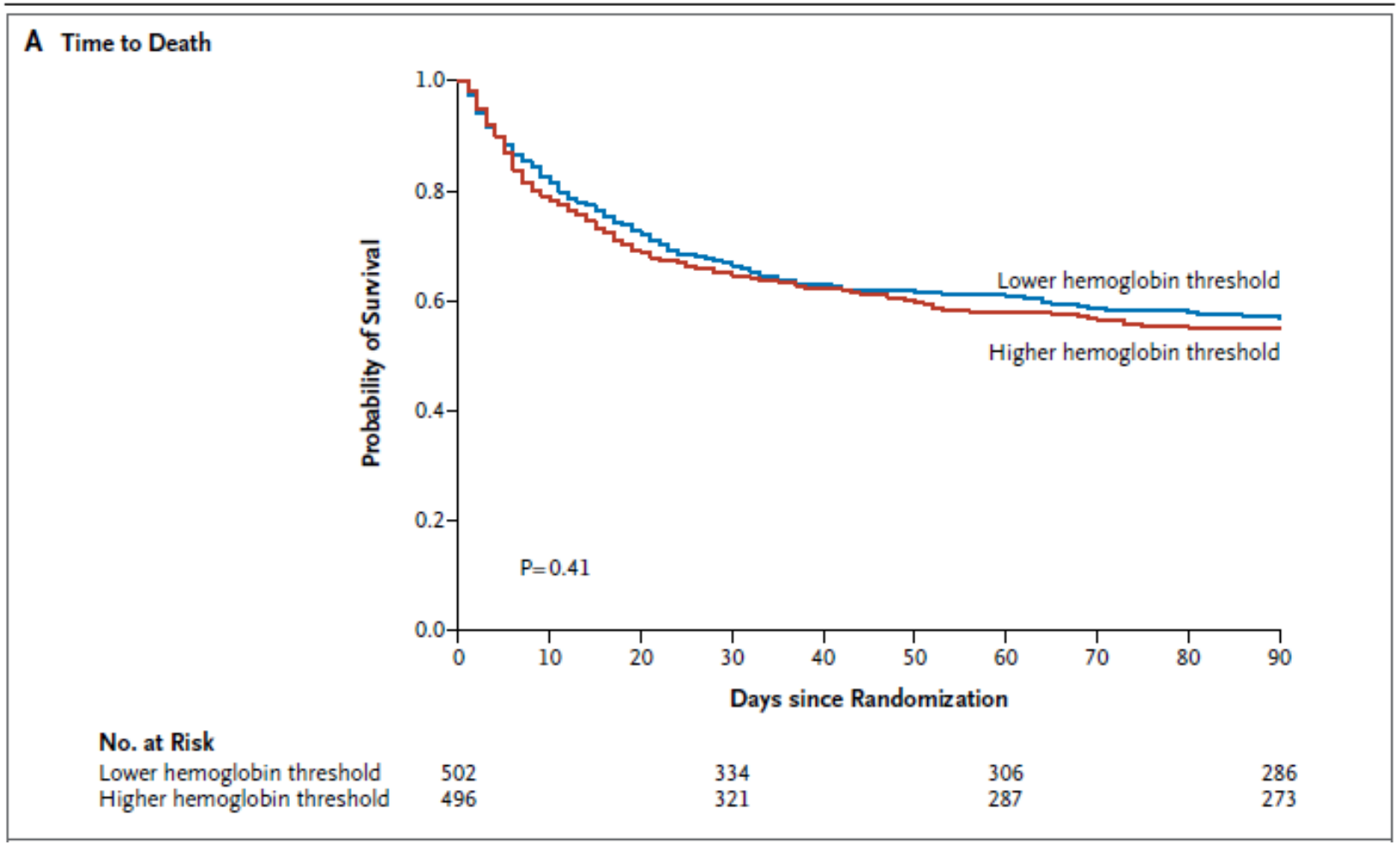
Subgroup	No. of Patients	Restrictive Threshold	Liberal Threshold	P Value for Interaction
		no. of patients with event/total no. (%)		
Age				0.004
<75 yr	2426	152/1218 (12.5)	131/1208 (10.8)	1.17 (0.91–1.50)
≥75 yr	2431	124/1210 (10.2)	172/1221 (14.1)	0.70 (0.54–0.89)
Sex				0.45
Female	1719	99/876 (11.3)	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)



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

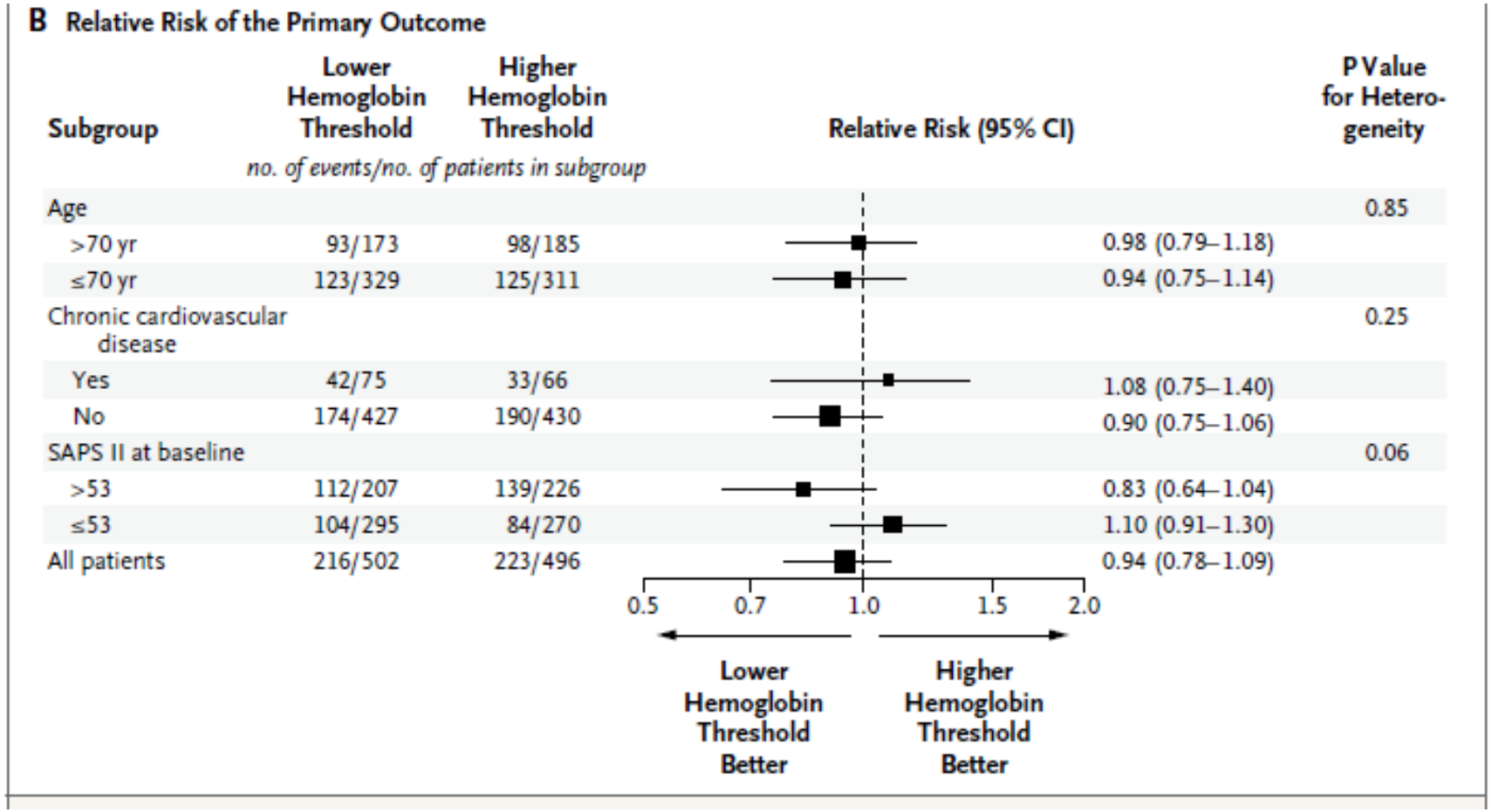
N Engl J Med 2017;377:2133-44.

TRISS 2014 RCT – 70 vs 90 g/L in sepsis



Holst et al. NEJM 2014

TRISS 2014 RCT – 70 vs 90 g/L in sepsis

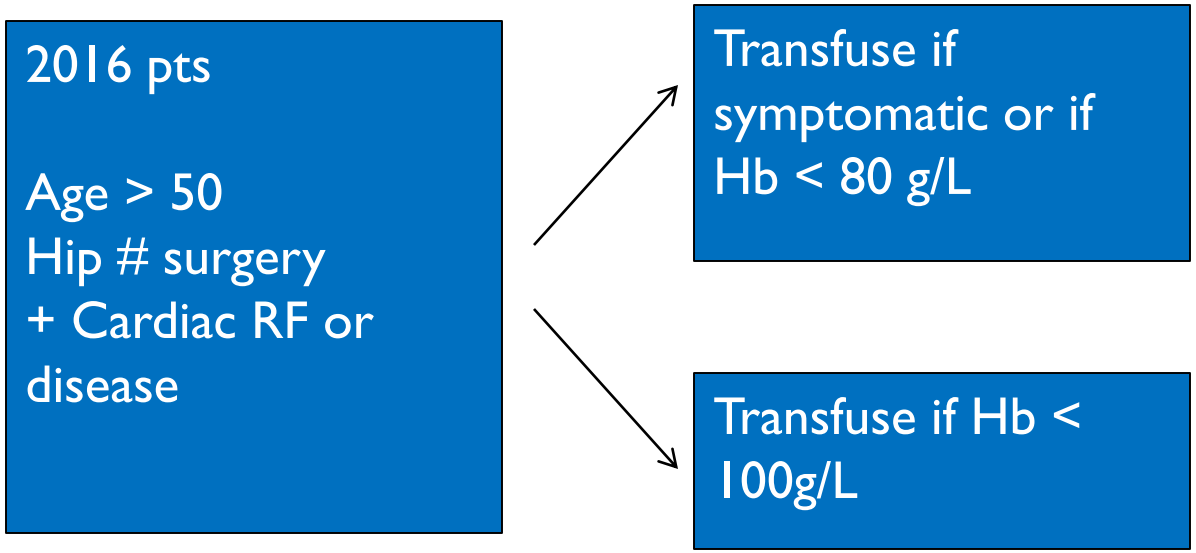


B Relative Risk of the Primary Outcome

Subgroup	Lower Hemoglobin Threshold	Higher Hemoglobin Threshold	Relative Risk (95% CI)	P Value for Heterogeneity
	no. of events/no. of patients in subgroup			
Age				0.85
>70 yr	93/173	98/185	0.98 (0.79–1.18)	
≤70 yr	123/329	125/311	0.94 (0.75–1.14)	
Chronic cardiovascular disease				0.25
Yes	42/75	33/66	1.08 (0.75–1.40)	
No	174/427	190/430	0.90 (0.75–1.06)	
SAPS II at baseline				0.06
>53	112/207	139/226	0.83 (0.64–1.04)	
≤53	104/295	84/270	1.10 (0.91–1.30)	
All patients	216/502	223/496	0.94 (0.78–1.09)	

Holst et al. NEJM 2014 epub

FOCUS Trial



Outcomes

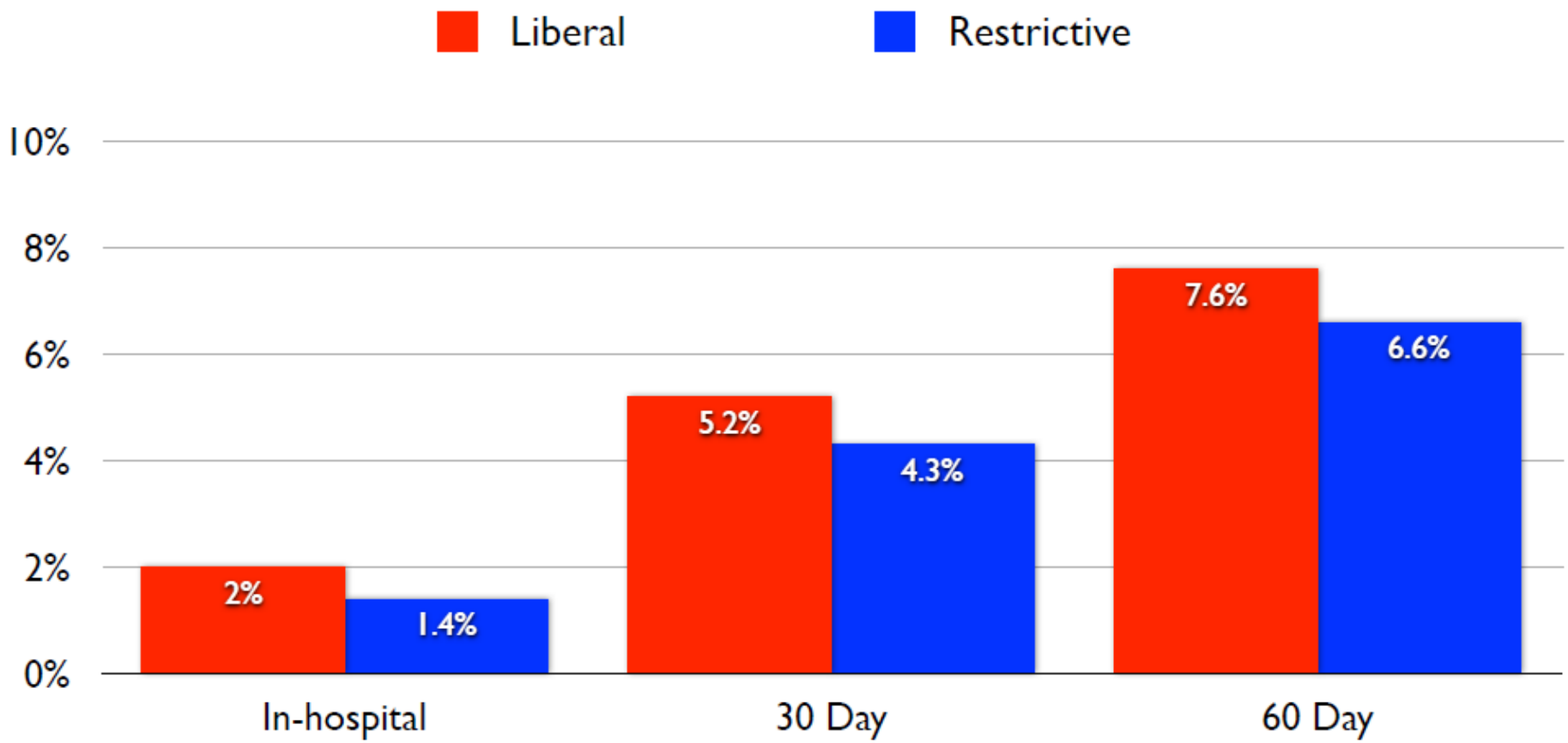
1°: 60 day mortality or inability to walk independently

2°: In-hospital outcomes, falls, fatigue, readmit to hospital, 60 day mortality

Median Age 82
Liberal group required 3x more RBCs

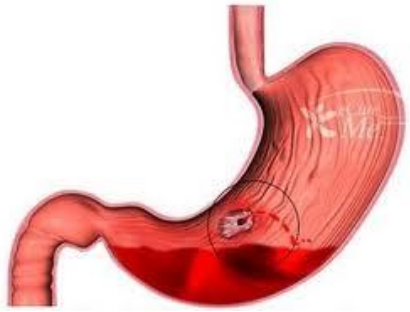
NEJM 2011;365(26):2453-62

Mortality



all p=NS

Acute UGI Bleeding



921 pts with severe UGIB

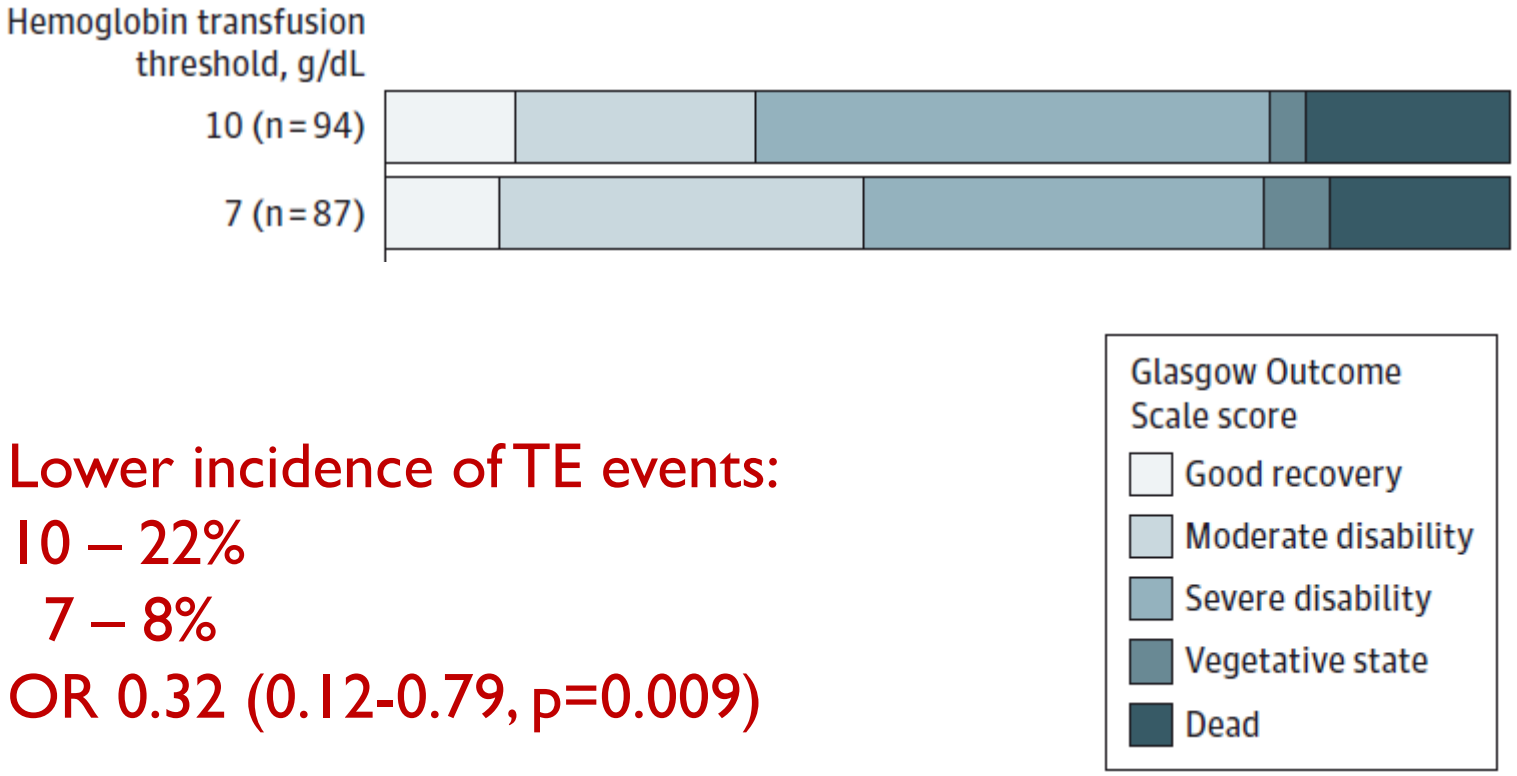
Restrictive Hb < 70 g/L

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

Traumatic Brain Injury



Lower incidence of TE events:

10 – 22%

7 – 8%

OR 0.32 (0.12-0.79, p=0.009)

JAMA. 2014;312(1):36-47. doi:10.1001/jama.2014.6490

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

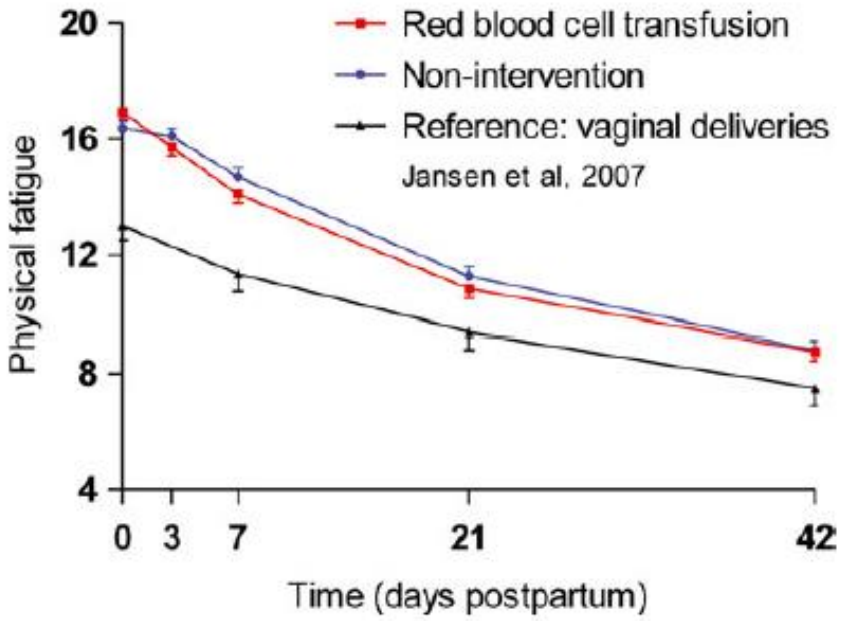


Table 2. Blood loss, haemoglobin concentration, and RBC transfusion

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

BJOG 2014;121:1005–1014.

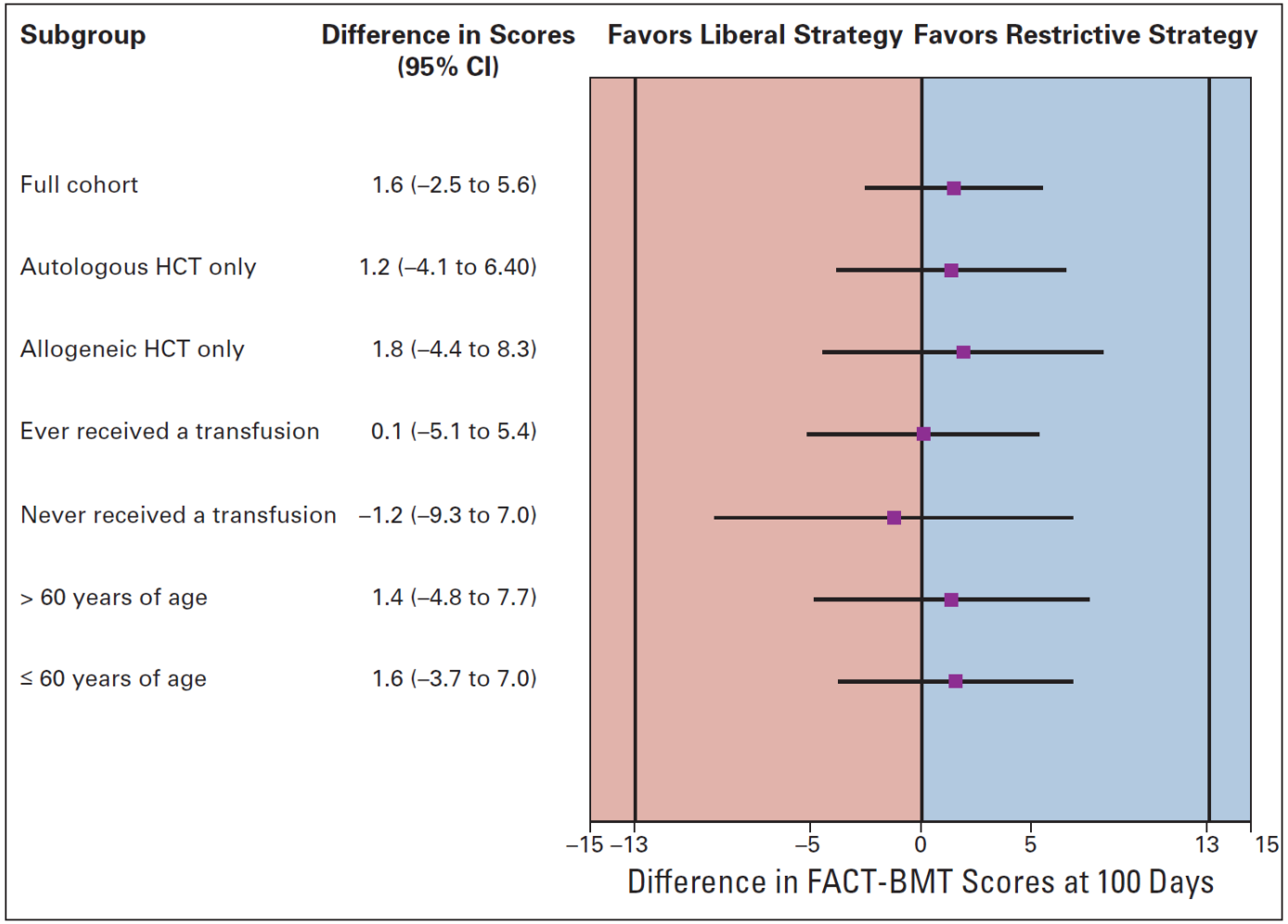
48

TRIST Study
(Triggers in patients undergoing HSCT)

- 300 adult patients
- Undergoing autologous or allogeneic HSCT
- Trigger 70 vs. 90 g/L
- Target 80-90 vs. 100-110 g/L
- Outcome QOL by FACT-BMT scale
- Mean pre-transfusion hemoglobin difference between groups was 13.7(±9.8) g/L
- RBC units transfused in the restrictive-strategy group vs. the liberal-strategy group [2(2-6) vs. 4(2-6), p=0.10]
- No difference in any clinical outcomes

Tay, J, et al. JCO 2020 May 1;38(13):1463-1473

TRIST Study



Tay, J, et al. JCO 2020 May 1;38(13):1463-1473

Huge difference in blood use (ie. costs)

TABLE A4. Use of Transfusion

	Restrictive Strategy					Liberal Strategy					
Variable	**No.**	**Median**	**IQR**	**Mean**	**SD**	**No.**	**Median**	**IQR**	**Mean**	**SD**	***P***
Full cohort	149					150					
RBC transfusion units	407	2	0-2	2.73	4.81	753	4	2-6	5.02	6.13	.0004
RBC transfusion episodes	234	1	0-2	1.57	2.96	407	2	1-3	2.71	3.33	.002
Duration of transfused RBC storage, days		17	13-23	18.46	7.27		20	15-25	19.95	7.52	.001
Platelet transfusion episodes		2	1-3	3.84	8.24		2	1-4	3.61	4.87	.77
Platelet transfusion units		2	1-3	4.11	9.73		2	1-4	3.75	5.44	.69
Pre-transfusion Hb (g/L)		69	67-75	70.90	7.44		86	83-88	84.61	6.38	< .0001
Difference of the mean pre-transfusion Hb (g/L)				13.71	6.77						
Threshold allocation minus pre-transfusion Hb (g/L)				−0.90	7.44				5.39	6.38	

Tay, J, et al. JCO 2020 May 1;38(13):1463-1473

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
- No patient group requires "fresh" blood

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

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 (or randomize to MINT)	<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!

START Study

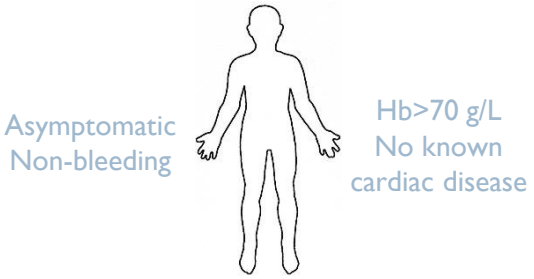
Screening by Technologists and Auditing to Reduce Transfusion

1,950 patients audited, 2,877 RBC transfused, Baseline 74% RBC units appropriate

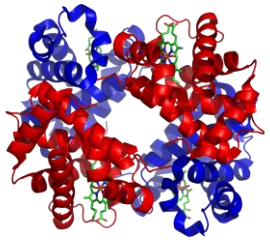
appropriateness increased (74% to 85%)

Decrease in RBCs transfused by 5000 U/10 months

Emergency physicians fell into the lowest range of appropriateness

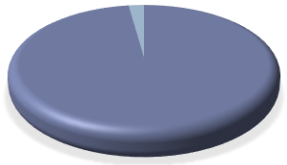


Clinical inpatient scenarios with lowest percentage of appropriate transfusions



Pre-transfusion Hb decreased (72 to 69)

Single-unit RBC transfusions increased (46 to 68%)



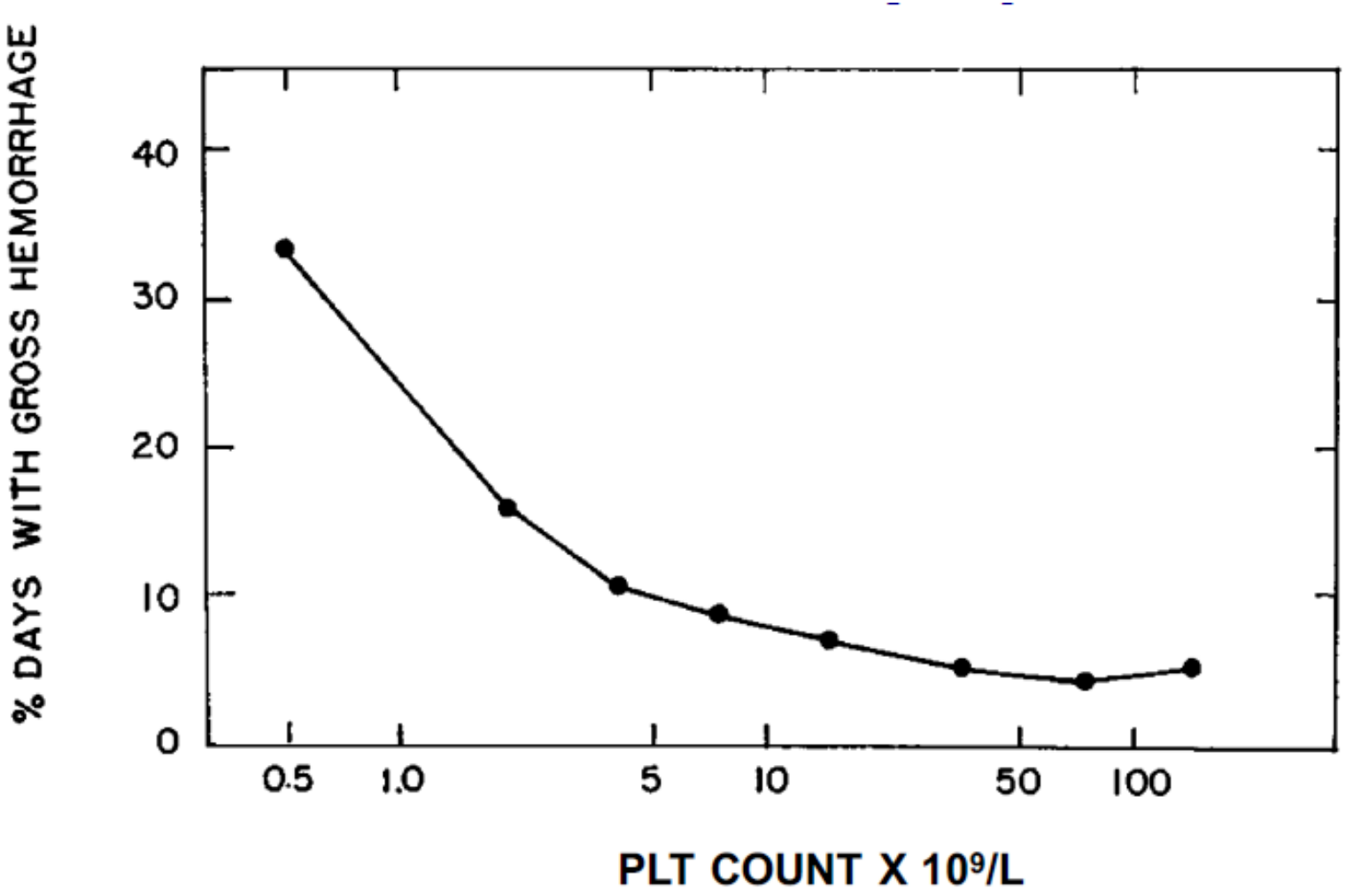
194 "under-transfusion events" (Hb <60) – 2.2% not explained by lab error or clear medical/religious reason

Intervention had no impact on length of stay, need for ICU support, or in-hospital mortality

Moving on to the PLT trials

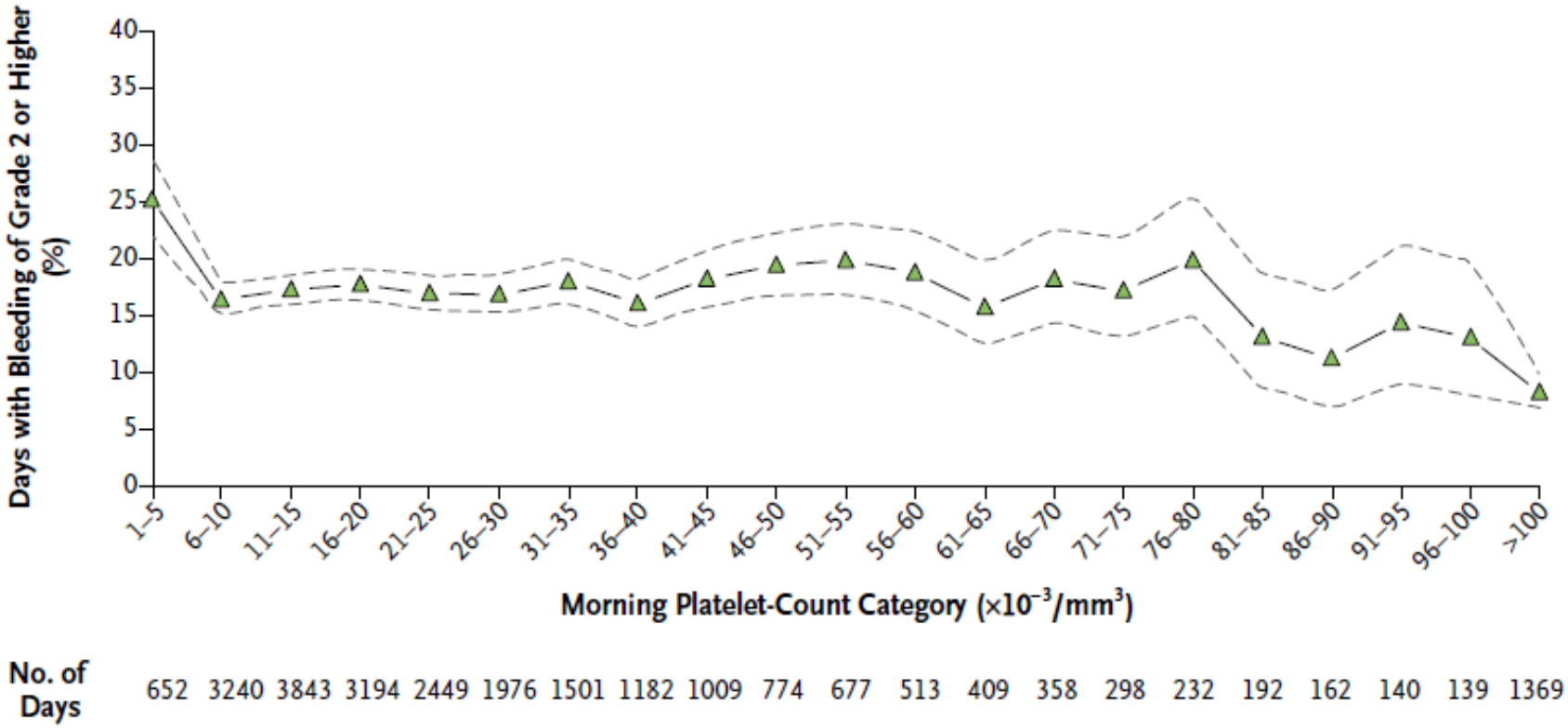
Again, this is science, not art

Do PLT transfusions prevent bleeding in patients with thrombocytopenia?



Gaydos et al. NEJM 1962; 266: 9

PLADO Trial



No escalation to <20 for febrile/septic/sick patients

Slichter S et al. NEJM 2010; 362: 600

Wandt Study (n= 396; AML or autoHSCT)

Bleeding	PLT prophylaxis	No prophylaxis	P value
Grade 2+ (minor)	65 (19%)	127 (42%)	<0.0001
Grade 3 (need Tx)	3 (1%)	7 (2%)	0.21
Grade 4 (CNS or Fatal)	4 (1%)	14 (5%)	0.02

No escalation to <20 for febrile/septic/sick patients

Wandt et al. Lancet 2012; 380: 1309

Wandt subgroup analysis

- AML (n=190)

	PLT prophylaxis	No prophylaxis	P value
Grade 2+	57 (24%)	98 (51%)	<0.0001
Grade 3	3 (1%)	6 (3%)	0.32
Grade 4	4 (2%)	13 (7%) **2 Fatal**	0.01

- AutoHSCT (n=201)

	PLT prophylaxis	No prophylaxis	P value
Grade 2+	8 (8%)	29 (28%)	0.0005
Grade 3	0 (0%)	1 (1%)	1.0
Grade 4	0 (0%)	0 (0%)	-

Wandt et al. Lancet 2012; 380: 1309

Stanworth Study (n= 600; Chemo for hematologic malignancy or autoHSCT)

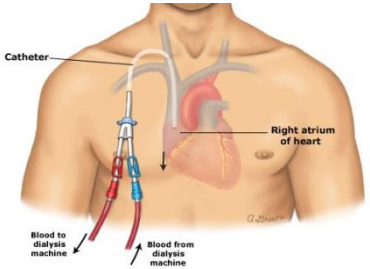
Bleeding	PLT prophylaxis	No prophylaxis	P value
Grade 2+ (minor)	128 (43%)	151 (50%)	0.06
Grade 3 (need Tx)	3 (1%)	7 (2%)	NS
Grade 4 (CNS or Fatal)	0 (0%)	2 (1%)	NS

For autoHSCT patients – no difference in bleeding rates (2-4)

No escalation to <20 for febrile/septic/sick patients

Stanworth S, et al. NEJM 2013; 369: 1771

Minor procedure: CVL



- Haas et al (n=3170 tunneled catheters; all pts)

PLT	n	Bleeds (>compression)
<20	42	0
20-49	302	0

- Zeidler et al (n=604 non-tunneled in AML pts)

PLT	n	Bleeds*	OR
<20	14	8 (57%)	2.84 (1.34-6.02)
20-49	156	50 (32%)	1.45
50-99	140	49 (35%)	1.48
>99	272	74 (27%)	1.00

***96% grade 1 (bruise); 4% grade 2 (pressure)**

Haas et al. J Vasc Int Rad 2010; 21:2
Zeidler et al. Transfusion 2011; 51: 2269

Minor procedure: LP

- 5223 LPs in children with ALL

PLT	N	Bleeds
≤20	199	0
21-50	742	0

- 195 LPs in adults

PLT	N	Bleeds	>500 RBC
21-30	35	0	6
31-50	40	0	4
51-100	43	0	3
>101	77	0	1

Howard et al. JAMA 2000; 284: 2222
Vavricka et al. Ann Hematol 2003; 82: 570

Minor procedures: Liver Biopsy

- 6613 Liver biopsies

PLT	No Bleeding	Bleeding	p
≤50	90 (97.8%)	2 (2.2%)	0.04
>50	6449 (99.5%)	31 (0.5%)	

- AASLD: management of patients scheduled for liver biopsy:
  - The decision to perform liver biopsy in the setting of abnormal laboratory parameters of hemostasis should continue to be reached as the result of local practice(s) and consideration of the risks and benefits of liver biopsy ***because there is no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted*** (Class I, Level C).
  - Platelets should be considered when levels are **<50-60 x 10^9/L** (both transcutaneously or transvenously) (Class I, Level C).

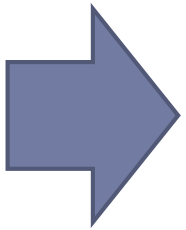
Boyum Mayo Clin Proc 2016; 91: 329
Rockey DC, et al. Hepatology. 2009;49(3):1017-44

Society of Interventional Radiology Guidelines

(Part 1 = Guideline on anticoagulant reversal covered later)

LOW RISK PROCEDURES – **NON-LIVER DISEASE**

Catheter change (e.g. nephrostomy)
Arterial interventions (e.g. embolotherapy)
Venous interventions
Dialysis access interventions
Spine injections/blocks
IVC filter
Lumbar puncture
Chest tube
Venous catheter placement
Paracentesis/thoracentesis
Abscess drain
Transjugular liver biopsy



No need to do INR/PTT or CBC!

If already done:
INR<2-3 okay
PLT>20 okay

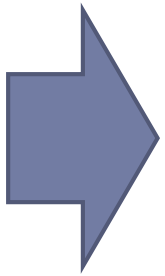
Patel IJ, et al. J Vasc Radiol 2019

Society of Interventional Radiology Guidelines

(Part 1 = Guideline on anticoagulant reversal covered later)

HIGH RISK PROCEDURES – **NON-LIVER DISEASE**

Ablations (e.g. solid organ, lung)
Arterial with >7F
Biliary interventions
Catheter directed thrombolysis
Deep abscess drain (e.g. lung, retroperitoneal)
Deep biopsies (e.g. retroperitoneal)
Gastrostomy placement
Portal vein intervention
Solid organ biopsy
Spine with risk of spinal/epidural bleed
TIPS
Nephrostomy
Venous interventions (intrathoracic, CNS)



INR <1.5-1.8
PLT >50

Patel IJ, et al. J Vasc Radiol 2019

Society of Interventional Radiology Guidelines

(Part 1 = Guideline on anticoagulant reversal covered later)

Table 4. Suggested Laboratory Thresholds for Performance of a Procedure in Patients with Chronic Liver Disease (52)

Procedure Risk	INR*	Platelet Count ($\times 10^9$/L)†	Fibrinogen (mg/dL)‡
Low	NA	> 20	> 100
High	< 2.5	> 30	> 100

= 1.0 g/L

Small print "error": 10 mg of vitamin K iv if INR>2.5 (NOTE: doesn't work in clinical studies – only use if patient not eating/on antibiotics)

Patel IJ, et al. J Vasc Radiol 2019

Serious bleeding: PATCH Trial

- Patients from 60 European hospitals
- Adults
- Non-traumatic supratentorial ICH
  - Excluded epidural, subdural, infratentorial, intraventricular
- Glasgow Coma Score > 7
- Within 6 hours on onset of symptoms
- On antiplatelets for at least last 7 days
- Platelet count >100
- Not planned for immediate surgical procedure
- RCT: ASA alone – one pool vs. nothing
- RCT: Clopidogrel +/- ASA – two pools vs. nothing

M Irem Baharoglu et al. Lancet 2016;387:2605-13

Outcome

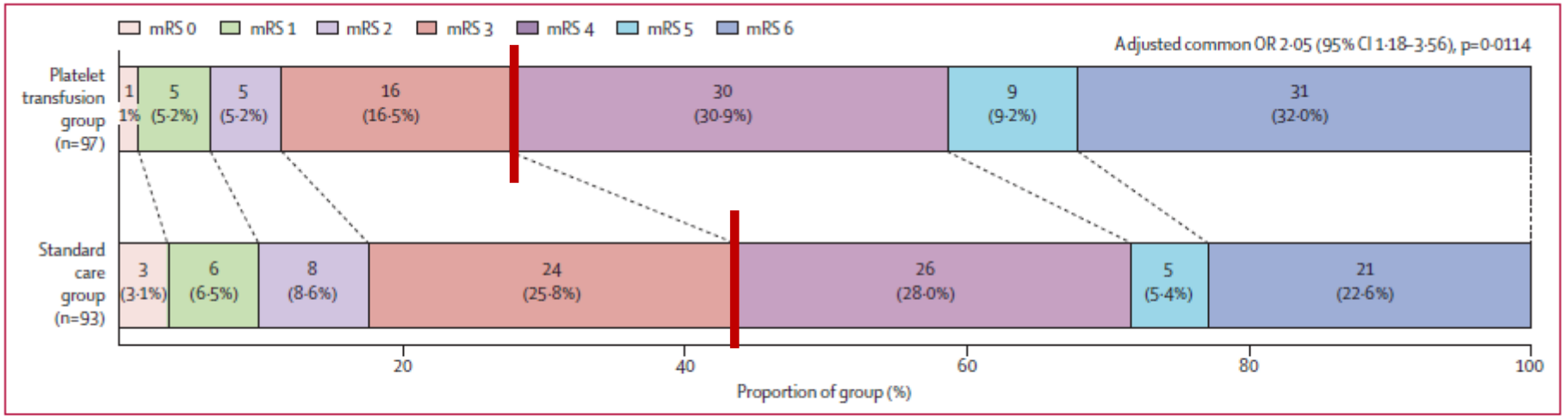


Figure 2: **Distribution of mRS score at 3 months**
mRS=modified Rankin Scale. OR=odds ratio.

0 - No symptoms.
1 - No significant disability. Able to carry out all usual activities, despite some symptoms.
2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3 - Moderate disability. Requires some help, but able to walk unassisted.
4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6 - Dead.

M Irem Baharoglu et al. Lancet 2016;387:2605-13

Serious adverse events

	Intention-to-treat population		
	Platelet transfusion group (n=97)	Standard care group (n=93)	Odds ratio (95% CI)
Any SAE	41 (42%)	27 (29%)	1·79 (0·98–3·27)
Any fatal SAE	24 (25%)	15 (16%)	1·71 (0·83–3·51)
SAE due to ICH	24 (25%)	13 (14%)	2·02 (0·96–4·27)
ICH enlargement	15 (15%)	13 (14%)	1·13 (0·50–2·52)
Brain oedema	5 (5%)	0	11·12 (0·61–204·97)
Brain herniation	2 (2%)	0	4·90 (0·23–103·33)
Intraventricular extension	6 (6%)	0	13·28 (0·74–239·24)
Hydrocephalus	3 (3%)	2 (2%)	1·45 (0·24–8·89)
SAE due to thromboembolism	4 (4%)	1 (1%)	3·96 (0·43–36·08)
Ischaemic stroke	1 (1%)	0	2·91 (0·12–72·26)
Myocardial infarction	1 (1%)	1 (1%)	0·96 (0·06–15·55)
Extremity embolism	2 (2%)	0	4·90 (0·23–103·34)
Pulmonary embolism	1 (1%)	0	2·91 (0·12–72·26)

More bleeding and more clotting?

Imbalance vs platelets are not a zero risk intervention?

M Irem Baharoglu et al. Lancet 2016;387:2605-13

Harmful for patients on antiplatelets with GI bleeding?

	Cases (N = 204)	Controls (N = 204)	Adjusted OR[a] (95% CI)
Recurrent GIB	29 (14%)	16 (8%)	1.47 (0.73–3.05)
Major adverse cardiovascular events	47 (23%)	26 (13%)	1.35 (0.74–2.49)
Myocardial infarction	46 (23%)	26 (13%)	1.32 (0.72–2.44)
Mortality	14 (7%)	3 (1%)	5.57 (1.52–27.1)
Length of stay >4 days	96 (47%)	68 (33%)	1.13 (0.71–1.79)

Liam Zakko, et al. Clin Gastroentrol Hepatol 2017 ;15:46-52

Annals of Internal Medicine

CLINICAL GUIDELINE

Platelet Transfusion: A Clinical Practice Guideline From the AABB

Richard M. Kaufman, MD; Benjamin Djulbegovic, MD, PhD; Terry Gernsheimer, MD; Steven Kleinman, MD; Alan T. Tinmouth, MD; Kelley E. Capocelli, MD; Mark D. Cipolle, MD, PhD; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Brenda J. Grossman, MD, MPH; Paul D. Mintz, MD; Barbara A. O'Malley, MD; Deborah A. Sesok-Pizzini, MD; Aryeh Shander, MD; Gary E. Stack, MD, PhD; Kathryn E. Webert, MD, MSc; Robert Weinstein, MD; Babu G. Welch, MD; Glenn J. Whitman, MD; Edward C. Wong, MD; and Aaron A.R. Tobian, MD, PhD

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Guidelines

Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia

JOURNAL OF CLINICAL ONCOLOGY

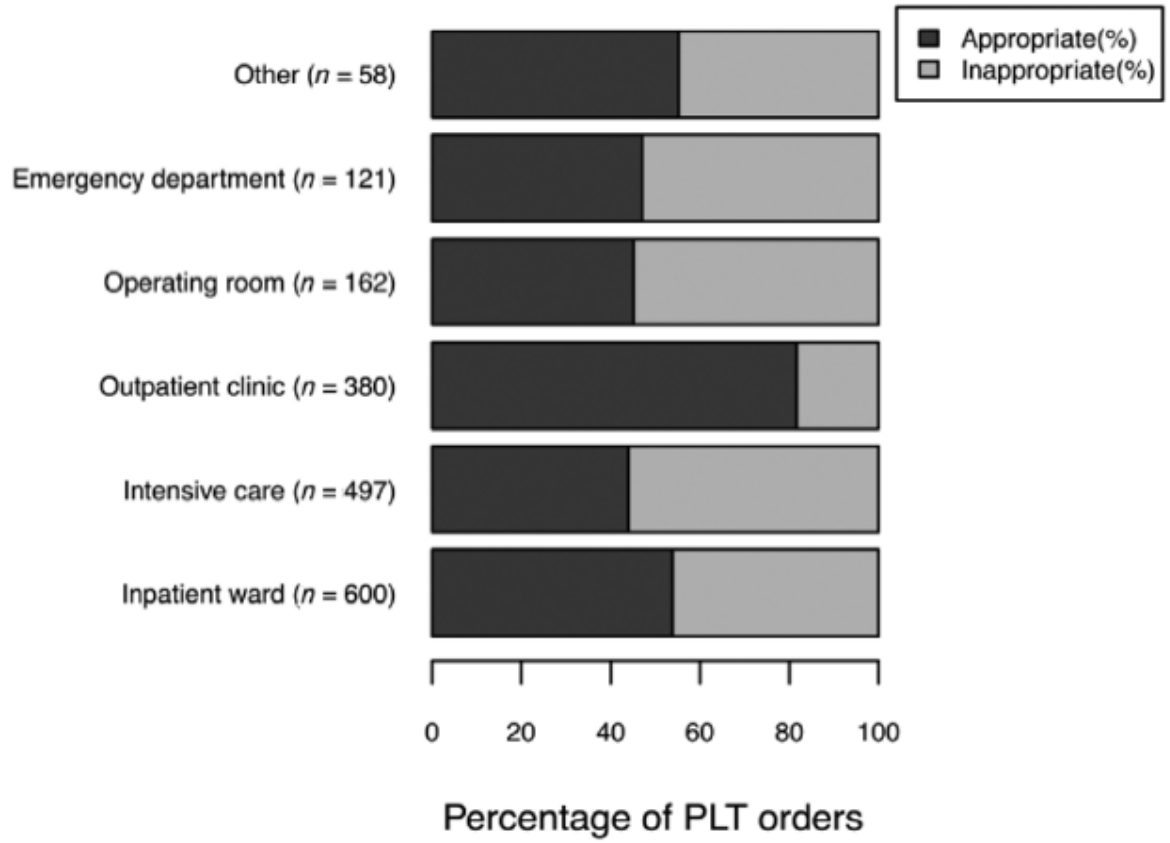
ASCO SPECIAL ARTICLE

Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Charles A. Schiffer, Kari Bohlke, Meghan Delaney, Heather Hume, Anthony J. Magdalinski, Jeffrey J. McCullough, James L. Omel, John M. Rainey, Paolo Rebulla, Scott D. Rowley, Michael B. Troner, and Kenneth C. Anderson

Provincial PLT audit results

C



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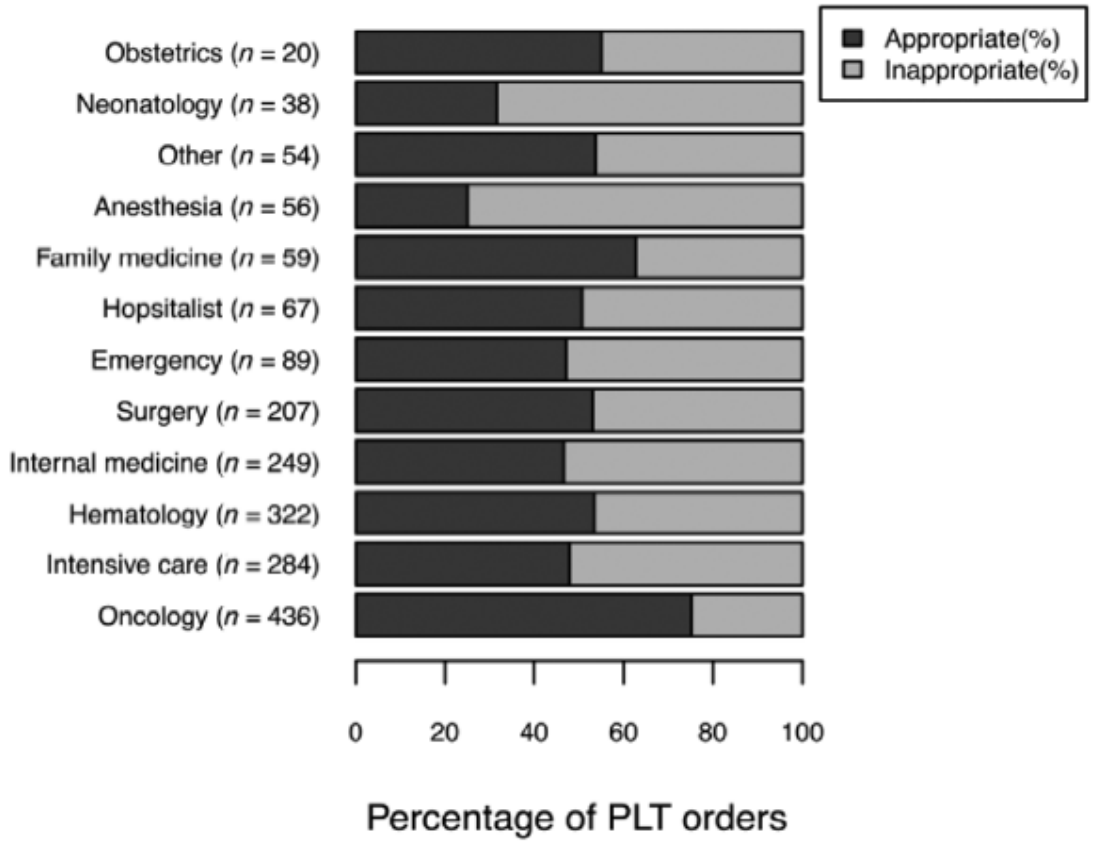
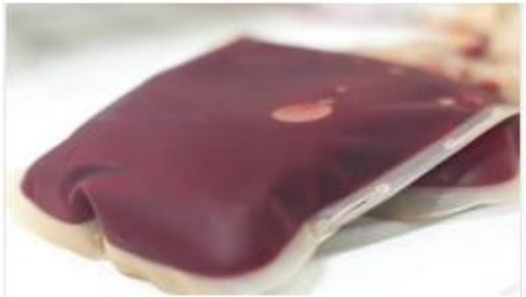


Transfusion. 2021;61:57–71.

Summary

- Why wouldn't you want to transfuse RBCs and PLTs to a patient?
  - RBC: TACO (2.5% >65), alloimmunization (women<45)
  - Platelets: Bacterial contamination
- When should you consider giving 1 unit of RBCs?
  - <50 for the very young, stable, reversible, Fe-def
  - <70 most patients
  - <70-80 cardiovascular (enroll in MINT trial)
- When should you give 1 pool of PLTs?
  - Only on days of bleeding, <10, <20, <50, <100
  - ITP: life-threatening hemorrhage

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!

Thank you for your attention

Questions and Criticisms Welcome