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- If you have questions, type them in the chat box at the bottom left hand side of your screen. They will be answered at the end of the presentation.
- This conference is being recorded for future use.
- The recording will be made available on the ASPHO website afterwards.

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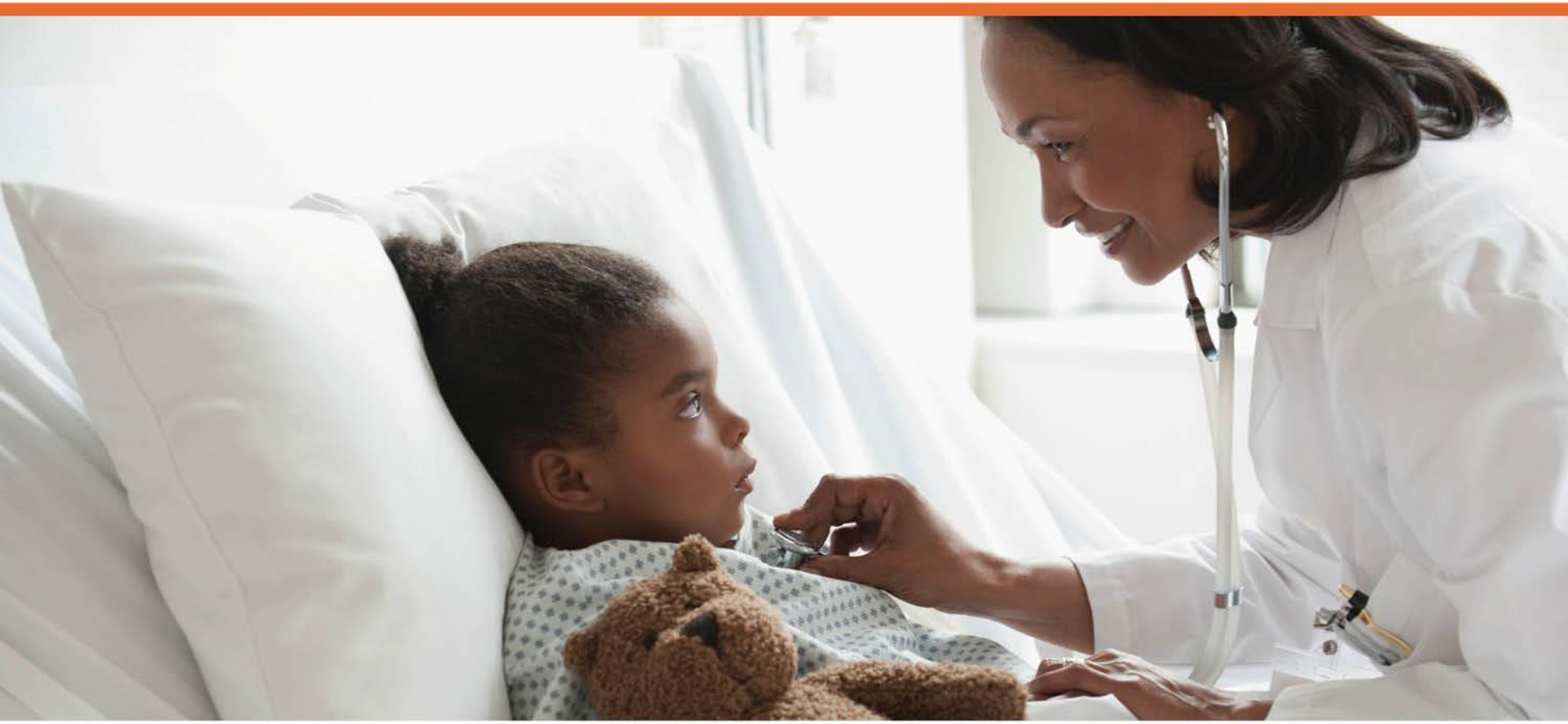
Evidence-based Decision Making for Transfusion Practices



Moderator: John Fargo, DO

Speaker: William Savage, MD PhD

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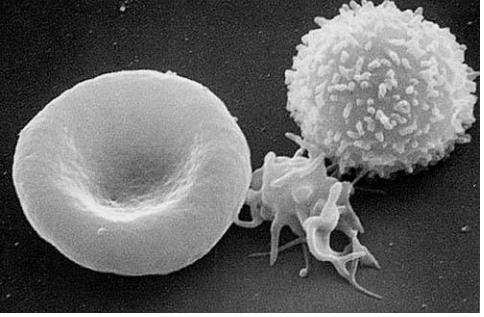
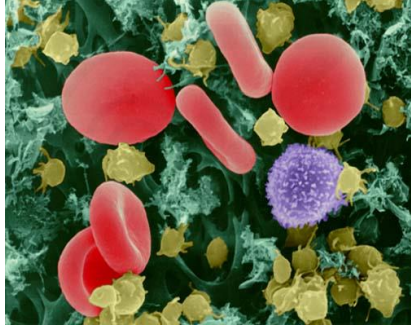
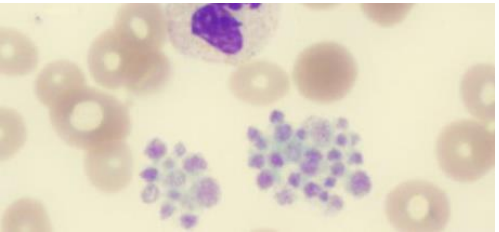




Evidence-based Decision Making for Transfusion

"What's the News on When to Transfuse"

Will Savage, MD, PhD



Disclosures

- Shire Pharmaceuticals (1/17/17-)
  - Full time-employee
  - Equity ownership
- PosterCast, LLC
  - Manager
  - Equity ownership

Objective

- Discuss recent evidence for blood product support scenarios
  - Indications
  - Dosing
  - Product selection
- Broad review with focus on newer clinical trial data

Outline

- Platelet Transfusion
  - Prophylactic threshold and dose
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

Outline

- Platelet Transfusion
  - Prophylactic threshold
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

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Gaydos et al., 1962 (NEJM)

- Retrospective review of 92 patients with ALL and AML starting at Dx.
- “Patients were followed till death”
- “There was no threshold”
- Manual plt counts

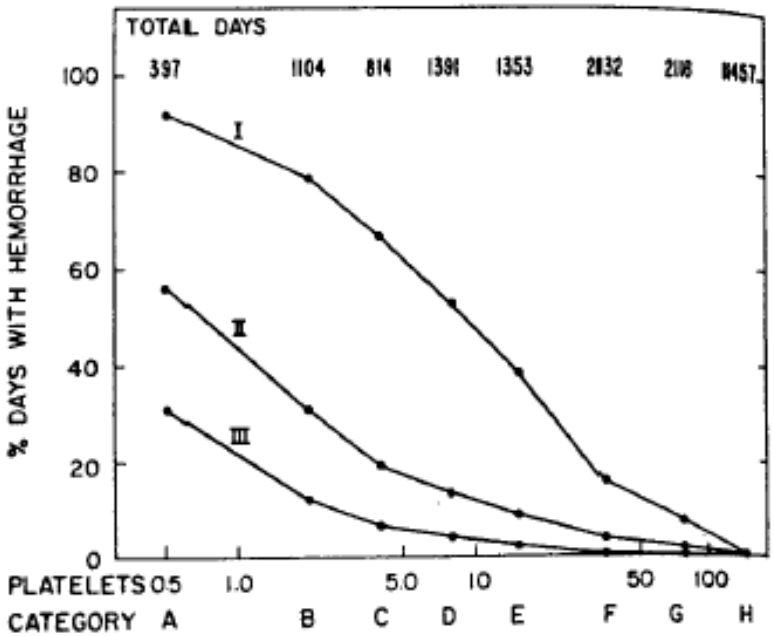

FIGURE 1. *Relation between Hemorrhage and Platelet Count.*

The percentage of days with hemorrhage for the 92 patients combined is shown for each of the 8 platelet-count categories. (Figures across the top are the total number of patient days in each of the categories.) Curve I shows data for all hemorrhagic manifestations. In Curve II skin hemorrhage and epistaxis are excluded. Curve III refers only to grossly visible hemorrhage.

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Platelet Transfusions Prevent Bleeding?

- 18 center observational study of 789 pts
- 2/3 of hemorrhage occurred with plt >20K

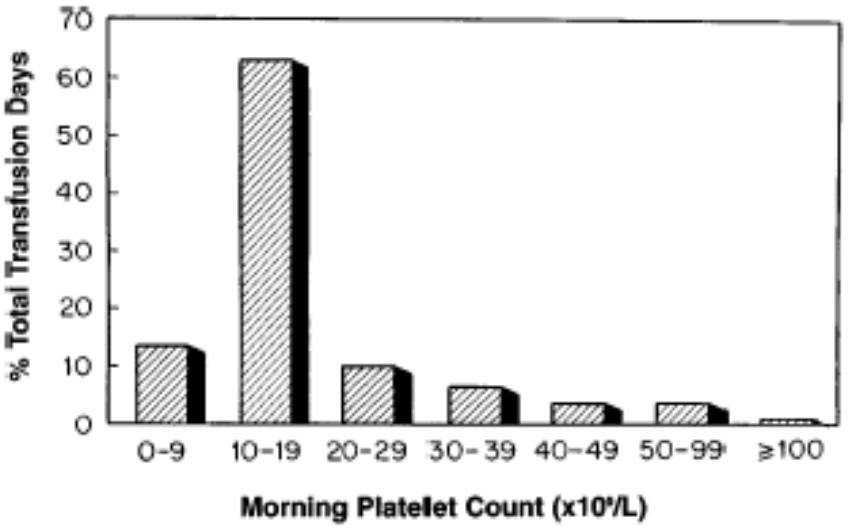

Fig 5. The distribution of platelet transfusion days by morning platelet count for all stem cell transplant patients (n = 789).

Platelet count on day of onset		
Not available	9	6
<5,000/L	5	3
6,000-10,000/L	9	6
11,000-15,000/L	17	12
16,000-20,000/L	10	7
21,000-50,000/L	58	41
>50,000/L	35	25

Bernstein et al. Blood. 1998

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Rebulla et al, 1997 (NEJM)

- RCT compared 10K to 20K triggers for plt Tx in AML induction (no M3 or 2° AML)
- Not specifically powered for non-inferiority (equivalence)

Rebulla, 1997

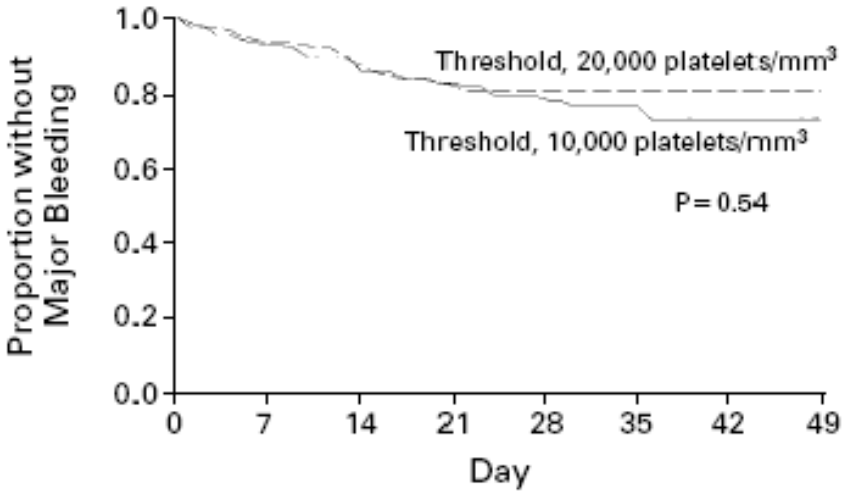

Figure 1. Proportion of Patients without Major Bleeding.

The relative risk of major bleeding was 1.1 in the group with a threshold of 10,000 platelets per cubic millimeter (95 percent confidence interval, 0.7 to 2.0) as compared with the group with a threshold of 20,000 platelets per cubic millimeter.

Type of Episode	Threshold, 10,000 Platelets/mm³	Threshold, 20,000 Platelets/mm³
	no. of episodes (no. of patients)	
Gastrointestinal bleeding	12 (10)	5 (3)
Hematuria	5 (5)	6 (4)
Metrorrhagia	3 (3)	2 (2)
Epistaxis requiring transfusion	2 (2)	2 (2)
Retinal hemorrhage with visual impairment	3 (3)	2 (2)
Gingival hemorrhage requiring transfusion	0	2 (2)
Hemoptysis	1 (1)	1 (1)
Nonfatal cerebral hemorrhage	0	1 (1)
Fatal cerebral hemorrhage	1 (1)	0
System or organ affected not reported	12 (10)	12 (10)
Total*	39 (29)	33 (24)

*Some patients had more than one type of episode.

The Platelet Dosing (PLADO) Trial
NEJM, 2010

+

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Modeling of Platelet Dosing

- Lower doses: less product utilization (good)
- Lower doses result in more time <10,000 (bad?)
- Identifying the balance between platelet utilization and bleeding risk

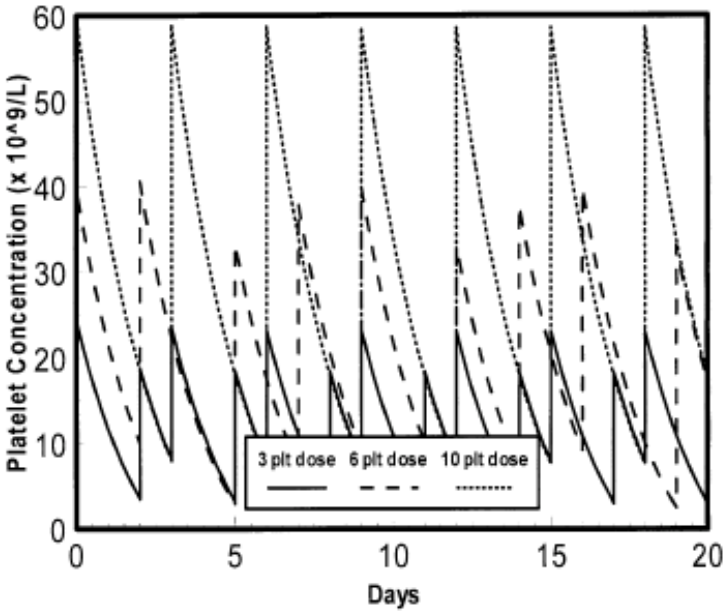

Fig 2. Total number of platelets transfused using 3 different prophylactic platelet transfusion doses: 3, 6, and 10 whole-blood–derived platelet units. (Reprinted with permission.[62])

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Surprising Result: Everyone Bled!

Table 3. Primary and Key Secondary End Points, According to Treatment Group.

Characteristic	Platelet Dose*					
	Low Dose (N=417)	P Value, Low vs. Medium Dose	Medium Dose (N=423)	P Value, Medium vs. High Dose	High Dose (N=432)	P Value, High vs. Low Dose
Primary end point						
≥1 Episode of bleeding of grade 2 or higher — % of patients	71	0.60	69	0.71	70	0.94
Secondary end points						
Highest grade of bleeding during study — % of patients		0.30		0.65		0.54
No bleeding or grade 1	30		32		30	
Grade 2	58		59		60	
Grade 3	9		7		8	
Grade 4	3		2		2	
Death from hemorrhage — no. of patients	0		0	1.00	1	1.00
No. of days with bleeding of grade 2 or higher		0.90		0.91		0.99
Median	1		1		1	
Interquartile range	0–4		0–4		0–4	
Days from randomization to onset of bleeding of grade 2 or higher		0.85		0.66		0.55
Median	7		7		8	
Interquartile range	3–18		3–19		3–19	

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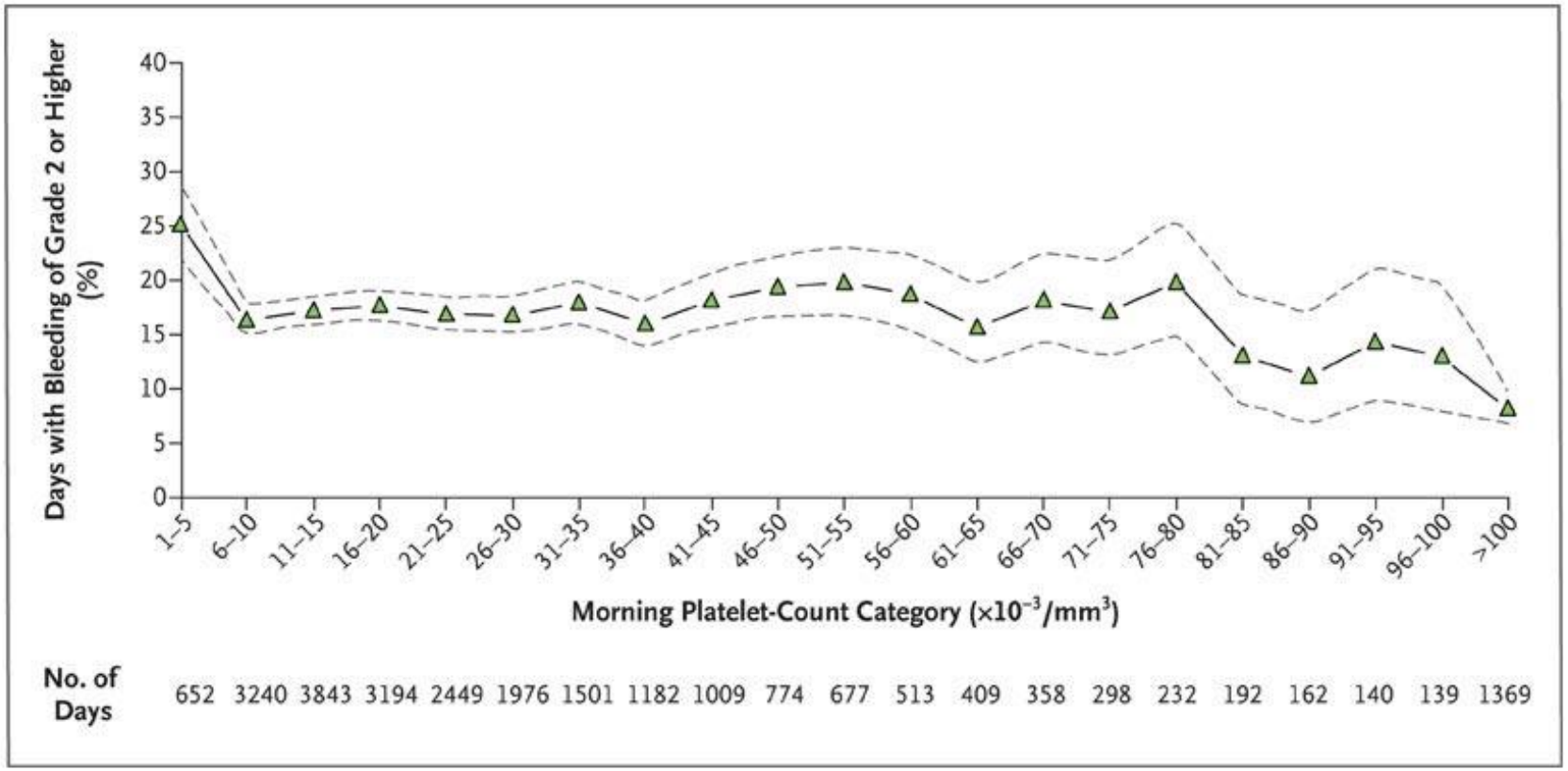
Bleeding vs. Platelet Count

Not clear that transfusing platelets is prophylactic

Platelets Matter

You're not as sick



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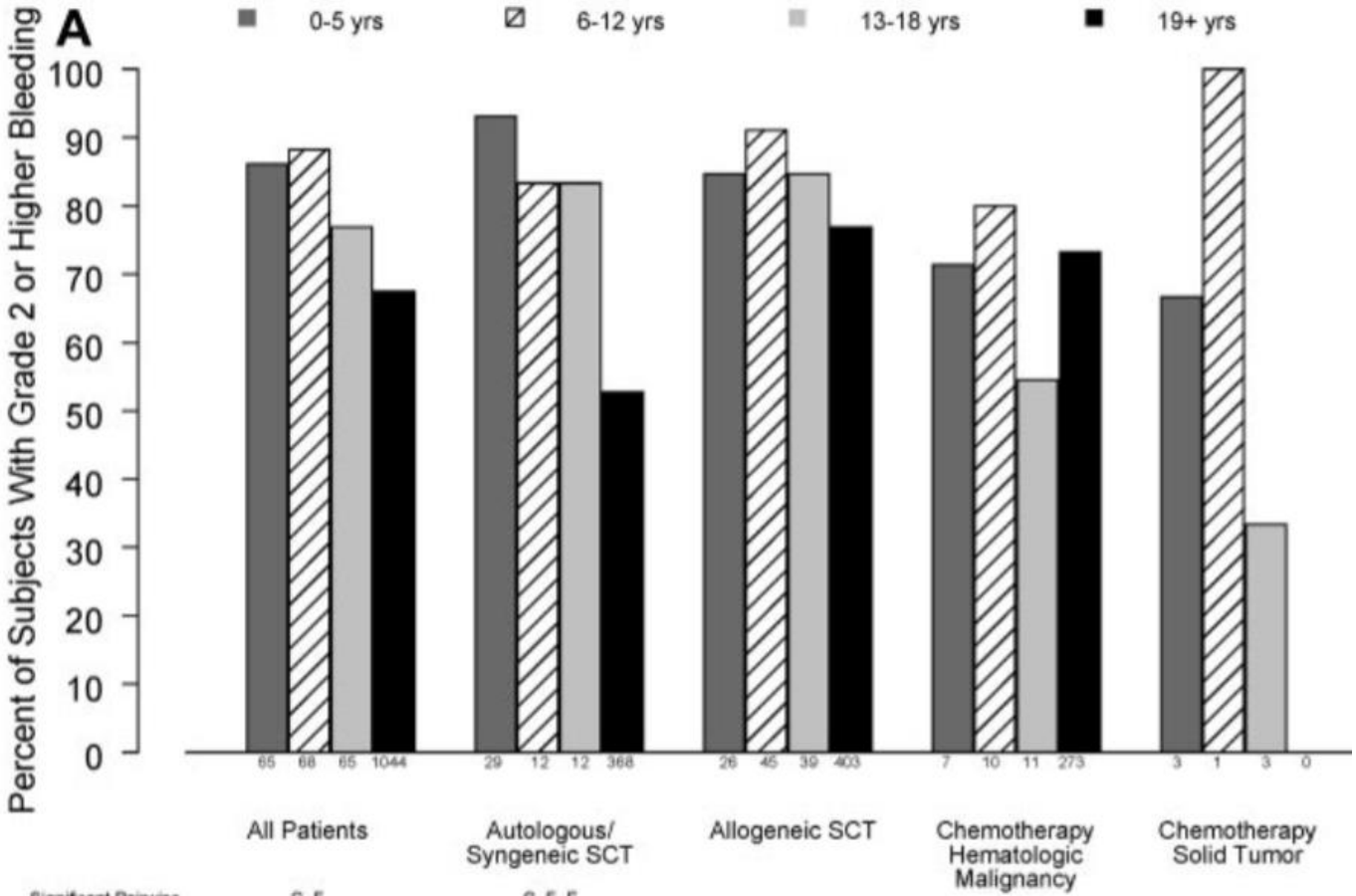
Peds PLADO Subgroup

CME article

Bleeding risks are higher in children versus adults given prophylactic platelet transfusions for treatment-induced hypoproliferative thrombocytopenia



Days ≥Grade 2

3 in peds

1 in adults

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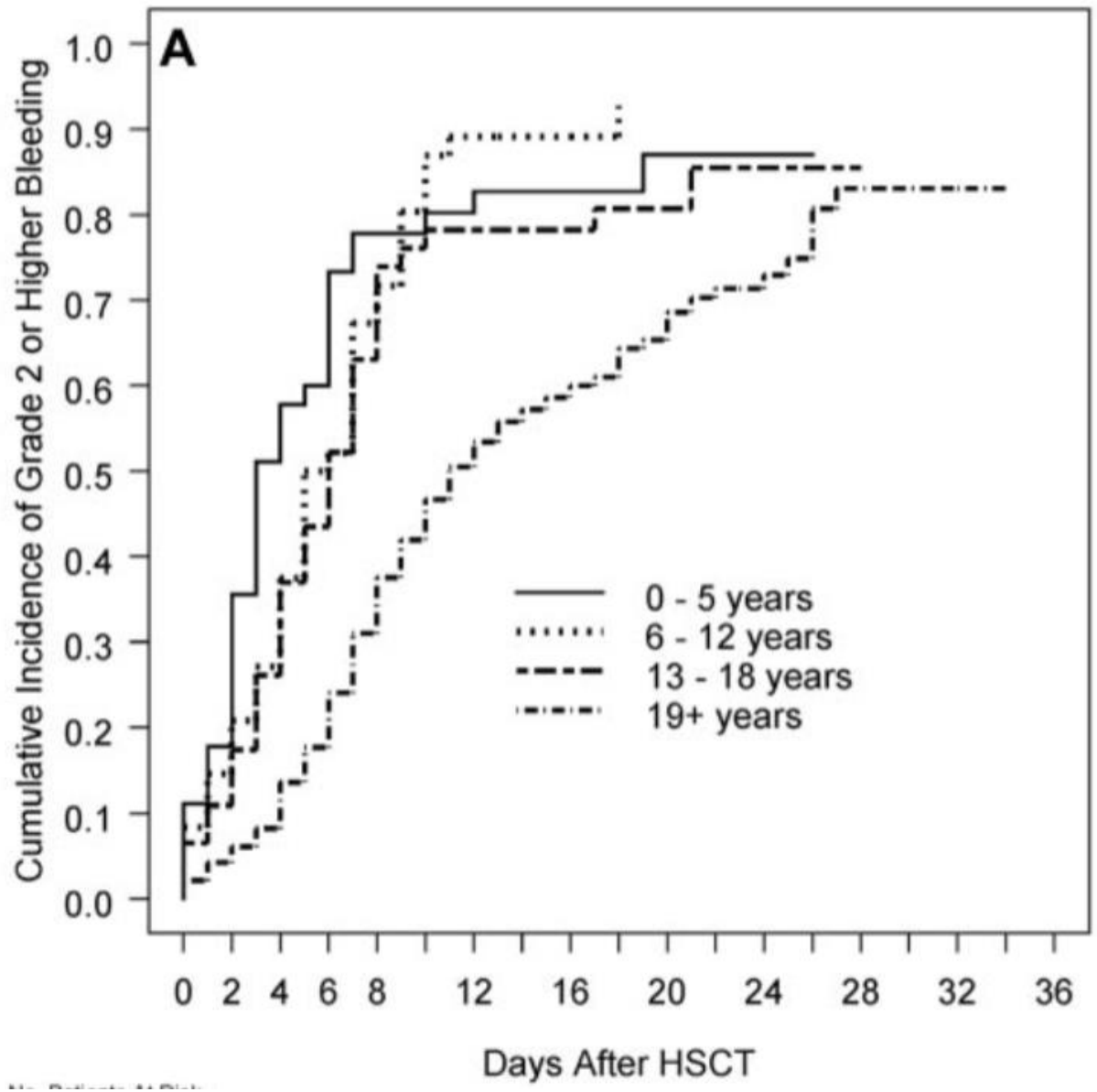
Peds PLADO Subgroup



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Is Platelet Tx Prophylaxis Needed? TOPPS Trial

ESTABLISHED IN 1812 MAY 9, 2013 VOL. 368 NO. 19

A No-Prophylaxis Platelet-Transfusion Strategy for Hematologic Cancers

- N=600
- Age ≥16 (mean=55)
- 70% auto HSCT

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Prophylactic Platelet Tx Slightly Better than No Tx

Outcome	No Prophylaxis (N=301)	Prophylaxis (N=299)	No Prophylaxis vs. Prophylaxis	P Value
Primary end point				
WHO grade 2, 3, or 4 bleeding — no. (%)	151 (50)	128 (43)	8.4 (1.7 to 15.2)†‡	0.06§
Secondary end points				
Highest grade of bleeding — no. (%)				
None or 1	149 (50)	170 (57)		
2	145 (48)	127 (43)		
3	4 (1)	1 (<1)		
4	2 (1)	0		
No. of days from randomization to first episode of grade 2, 3, or 4 bleeding	17.2±12.8	19.5±12.6	1.30 (1.04 to 1.64)¶	0.02‖
Receipt of platelet transfusions¶				
≥1 transfusion — no. (%)	176 (59)	266 (89)	0.14 (0.09–0.23)‖	<0.001
No. of transfusions/patient	1.7±2.6	3.0±3.2	0.62 (0.51–0.74)§	<0.001
No. of platelet units transfused/patient	1.9±3.3	3.2±3.6	0.67 (0.55–0.82)§	<0.001

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TOPPS Trial: Auto vs. Allo Txp

Outcome	No Prophylaxis (N=301)	Prophylaxis (N=299)	No Prophylaxis vs. Prophylaxis	P Value
Bleeding events of grade 2, 3, or 4 according to treatment and type of cancer — no./total no. (%)				
Treatment				
Autologous stem-cell transplantation	99/210 (47)	95/210 (45)	2.3 (–5.7 to 10.3)†	
Chemotherapy	52/90 (58)	33/88 (38)	20.0 (7.9 to 32.2)†	0.04§§
Type of cancer				
Acute myeloid leukemia or acute lymphoid leukemia	37/60 (62)	21/56 (38)	24.2 (9.6 to 28.9)†	
Lymphoma or myeloma	107/226 (47)	100/227 (44)	3.3 (–4.4 to 11.0)†	
Chronic myeloid leukemia or other cancer	7/14 (50)	7/15 (47)	3.3 (–27.2 to 33.9)†	0.10§§

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AABB Platelet Tx Guidelines 2015

- For prophylactic plt tx if <10K
  - Strong, moderate quality
- For prophylactic plt tx if <20K for central venous catheter
  - Weak, low quality
- For prophylactic plt tx if <50K for major surgery (non-neuro) or lumbar puncture
  - Weak, very low quality

Kaufman et al. *Ann Intern Med*. 2015.

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Prophylactic Platelet Tx Points

- Platelets ≠ hemostasis
- Platelets + humoral factors ≠ hemostasis
- Platelets + humoral factors + vascular integrity = hemostasis
- Platelets, coag times/factors are easy to measure but aren't the whole story

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Outline

- Platelet Transfusion
  - Prophylactic threshold
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

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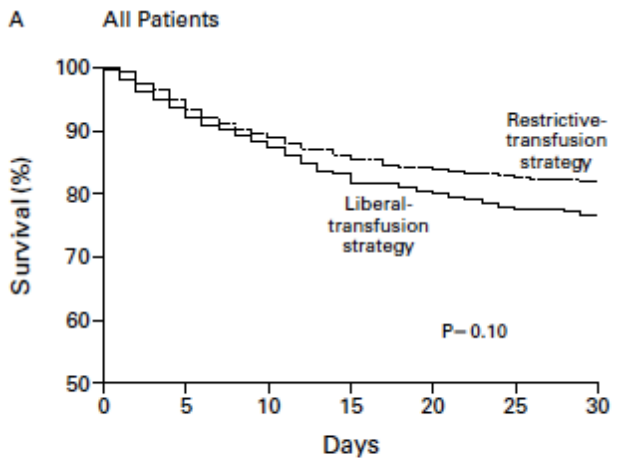
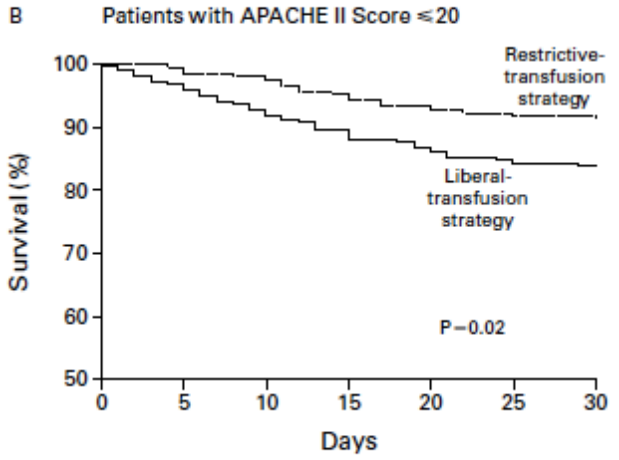
Considerations for Transfusing RBCs

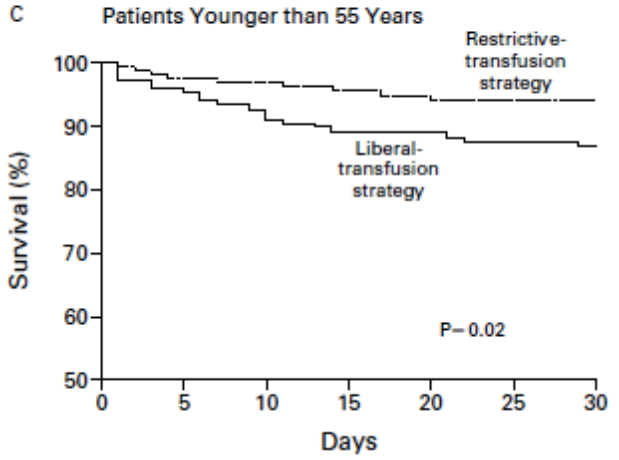
- Symptoms
  - Dyspnea
  - Tachycardia
  - ? Fatigue
- Degree of anemia
- Patient/Family wishes
- Comorbidities
- Clinical status
- Outpatient status

When to Transfuse: RBCs

- TRICC study (adults)
  - n=838 randomized to restrictive (keep hgb>7) or liberal (keep hgb>10)
  - Outcome: 30d survival
  - 82% intubated, 37% pressors







TRIPICU

- N=637 randomized
  - Mean age: 3y
  - Restrictive (keep hgb>7)
  - Liberal (keep hgb>9.5)
- Outcome is new/progressive MODS at 28d
- 12% incidence, both groups
- Mortality: equivalent
- 44% fewer transfusions with restrictive

Lacroix et al. *NEJM*. 2007.

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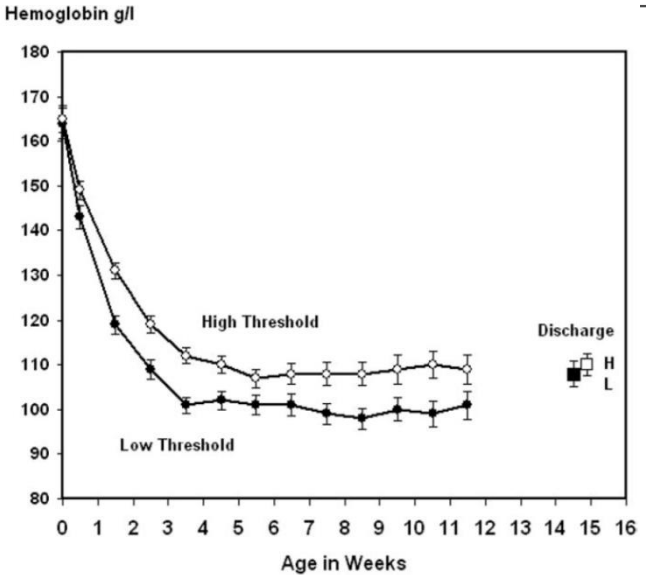
- ELBW (<1000g, n=458)

Table I. Hemoglobin threshold levels (g/L) triggering RBC transfusion

		Low threshold		High threshold	
Age in days	Blood sampling	Respiratory support	No respiratory support	Respiratory support	No respiratory support
1-7	Capillary	≤115	≤100	≤135	≤120
	Central	≤104	≤90	≤122	≤109
8-14	Capillary	≤100	≤85	≤120	≤100
	Central	≤90	≤77	≤109	≤90
≥15	Capillary	≤85	≤75	≤100	≤85
	Central	≤77	≤68	≤90	≤77



Kirpalani et al. *J Peds*. 2006.

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Table V. Primary outcome

Outcome cluster	Low threshold	High threshold	Treatment effect* (95% CI)	*P* value
Composite primary				
Death, severe ROP, BPD, or head ultrasound brain injury	165/223 (74.0%)	159/228 (69.7%)	OR: 1.30 (0.83, 2.02) RD: 2.7% (−3.7%, 9.2%)	.25
Individual components				
Death	48/223 (21.5%)	40/228 (17.5%)	OR: 1.38 (0.84, 2.27) RD: 2.6% (−3.5%, 8.8%)	.21
Survived with severe ROP	33/175 (18.9%)	33/188 (17.6%)	OR: 1.27 (0.71, 2.26) RD: 1.1% (−4.6%, 6.8%)	.42
Survived with BPD	101/175 (57.7%)	103/188 (54.8%)	OR: 1.18 (0.76, 1.85) RD: 3.9% (−4.6%, 12.4%)	.46
Survived with head ultrasound brain injury	22/175 (12.6%)	30/188 (16.0%)	OR: 0.86 (0.53, 1.39) RD: −3.3% (−9.9%, 3.4%)	.53

Kirpalani et al. *J Peds*. 2006.

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FOCUS

- Hip surgery (n=2016); Mean age: 81y
- 63% cardiovascular dz
- Primary outcome: death or inability to walk independently

Table 3. Outcomes at 30 Days and 60 Days.*

Variable	30-Day Period		
	Liberal Strategy (N=1007)	Restrictive Strategy (N=1009)	Odds Ratio (99% CI)
	no./total no. (%)		
Death or inability to walk independently	459/995 (46.1)	481/1000 (48.1)	0.92 (0.73 to 1.16)
Inability to walk independently	407/995 (40.9)	438/1000 (43.8)	
Death	52/995 (5.2)	43/1000 (4.3)	1.23 (0.71 to 2.12)

Carson et al. *NEJM*. 2011.

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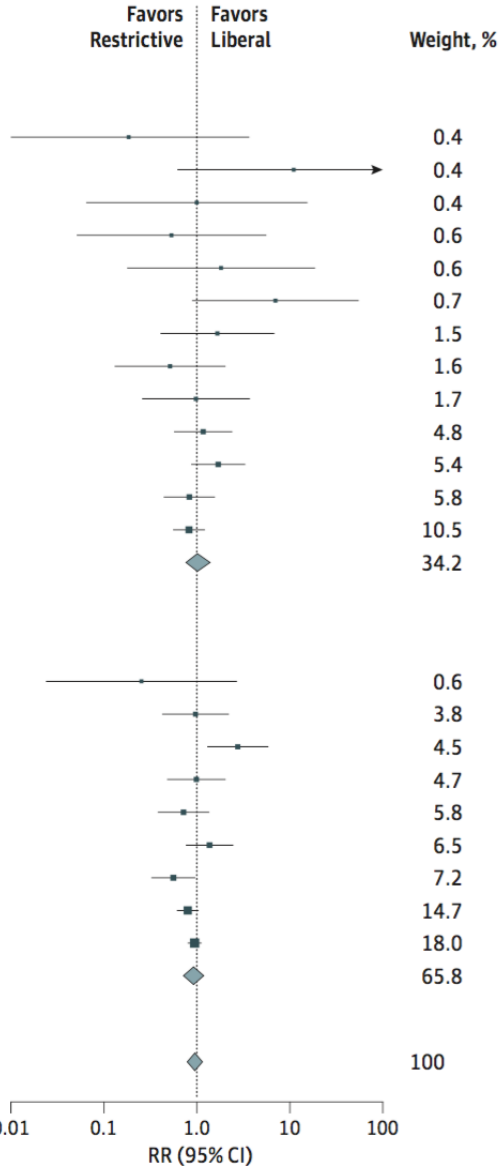
AABB Systematic Review-Threshold

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)
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: $\chi^2_1=0.34$; $P=.56$; $I^2=0\%$					



Carson et al. *JAMA*. 2016

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RBC Transfusion Threshold

- No clinical trial evidence to support higher threshold for transfusion
- Priority placed on avoiding transfusion, i.e. favor restrictive strategy

Outline

- Platelet Transfusion
  - Prophylactic threshold
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

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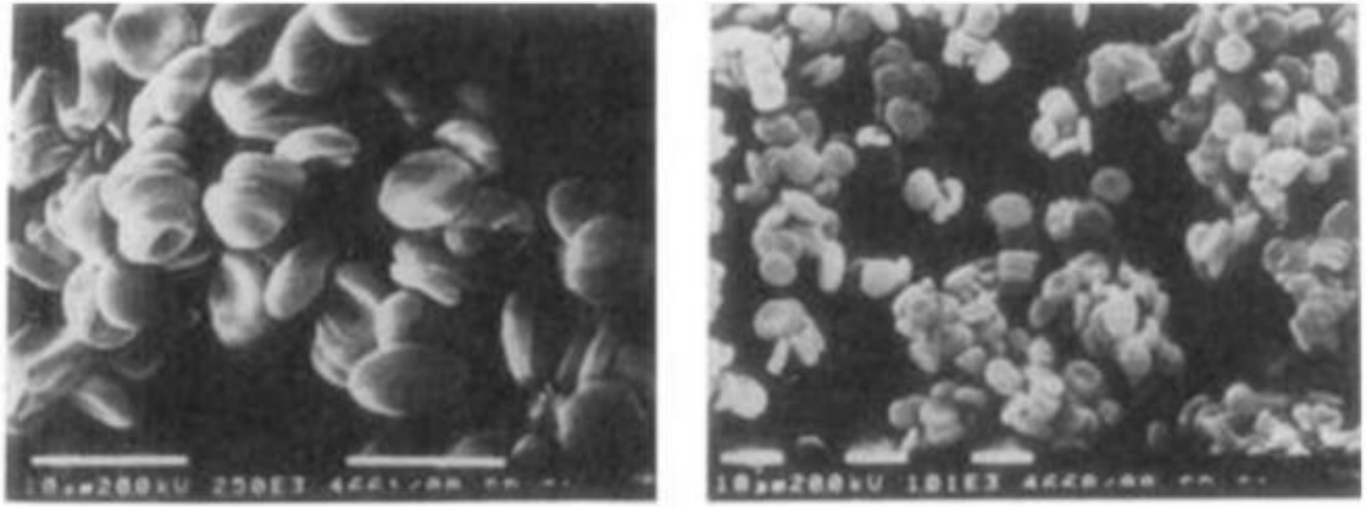
Storage Lesion

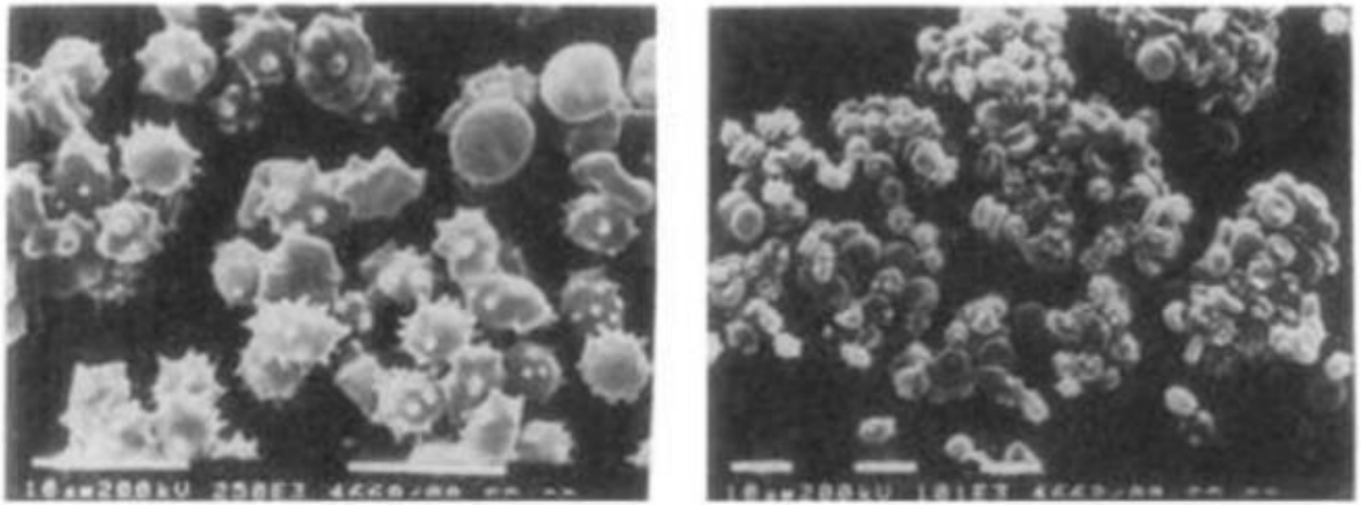
- Myriad biochemical and structural changes
- NO
  - Free hemoglobin (scavenge NO)
  - Asymmetric dimethyl arginine (inhibit NO synth)
- Decrease 2,3 BPG
- Inflammatory cytokine induction
- Promotion of bacterial growth
- Increased thrombin generation

A



Day 1

B



Day 21

Hovav et al. *Transfusion*. 1999.

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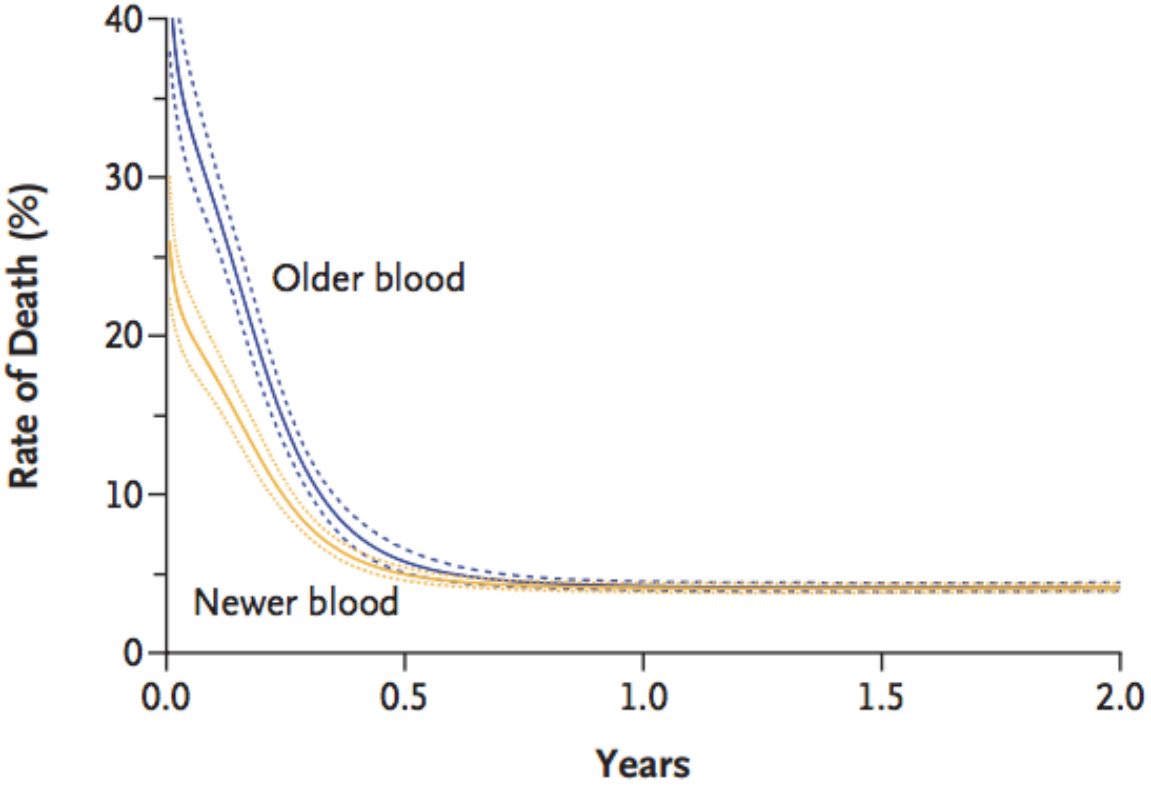
The Koch Study



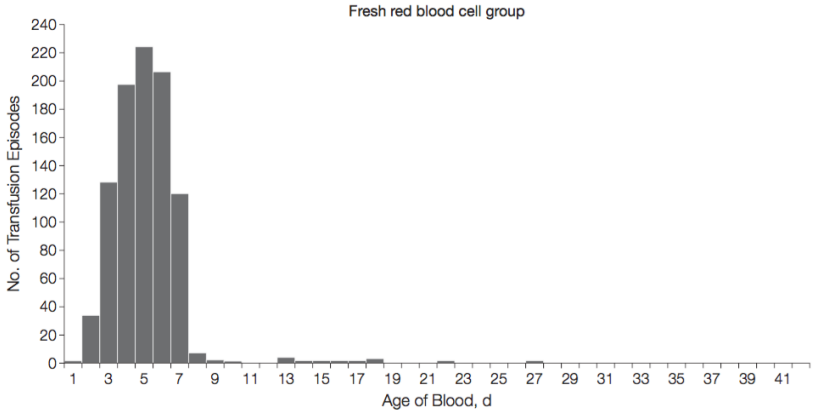
Cardiac surgery, 1998-2006
Exclusively +/-14d storage
Propensity score adjusted

ABO imbalanced
Not adjusted for time (practice change)

Koch, CG et al. *NEJM* 2008.

ARIPI Trial- Neonates

Figure 2. Distribution of Age of Red Blood Cell Transfusion Episodes in Fresh and Standard Groups



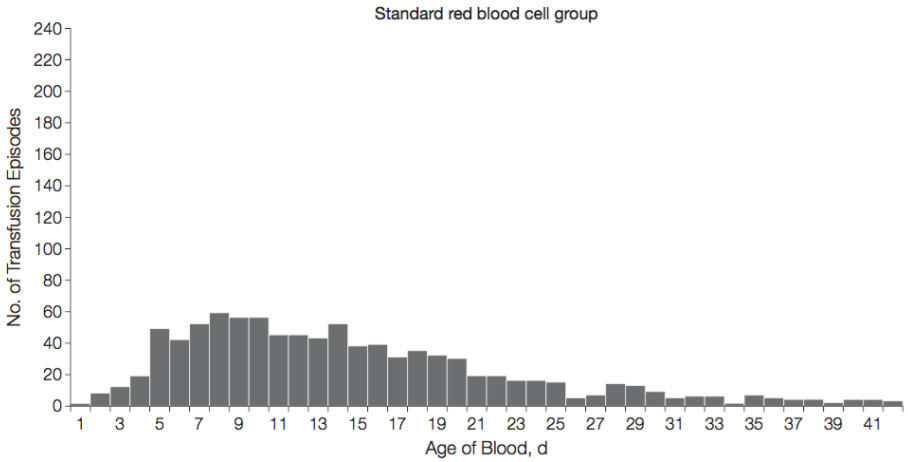


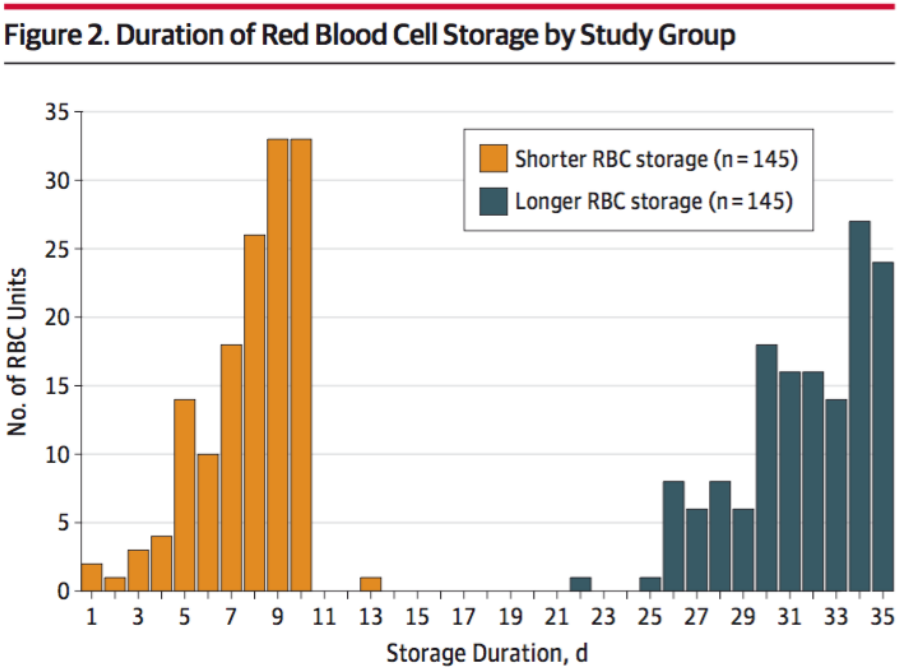
Table 4. Primary Outcomes

Primary Outcomes	No. (%) Standard Red Blood Cell Group (n = 189)	No. (%) Fresh Red Blood Cell Group (n = 188)	Relative Risk (95% CI)
Necrotizing enterocolitis (Bell criteria stage ≥2)	15 (7.9)	15 (8.0)	1.00 (0.48-2.12)
Intraventricular hemorrhage (Papile criteria grade ≥3)	11 (5.8)	18 (9.6)	1.65 (0.80-3.39)
Retinopathy of prematurity (stage ≥3)	26 (13.8)	23 (12.2)	0.89 (0.53-1.50)
Bronchopulmonary dysplasia	63 (33.3)	60 (31.9)	0.96 (0.72-1.28)
Death	31 (16.4)	30 (16.0)	0.97 (0.61-1.54)
Composite primary outcome: any of above	100 (52.9)	99 (52.7)	1.00 (0.82-1.21)

Fergusson et al.
JAMA. 2012

TOTAL: Ugandan PICU

- ≤10 vs 25-35 day
- N=290, Age 0.5-5y
- Mean Hgb 3.7
- Outcome: Lactate <3 mmol/L @8h
- Dx: 81% malaria; 13% SCD
- No:
  - Pressors
  - Intubation
  - Dialysis



Dhabangi et al. *Lancet*. 2015

TOTAL: Ugandan Children

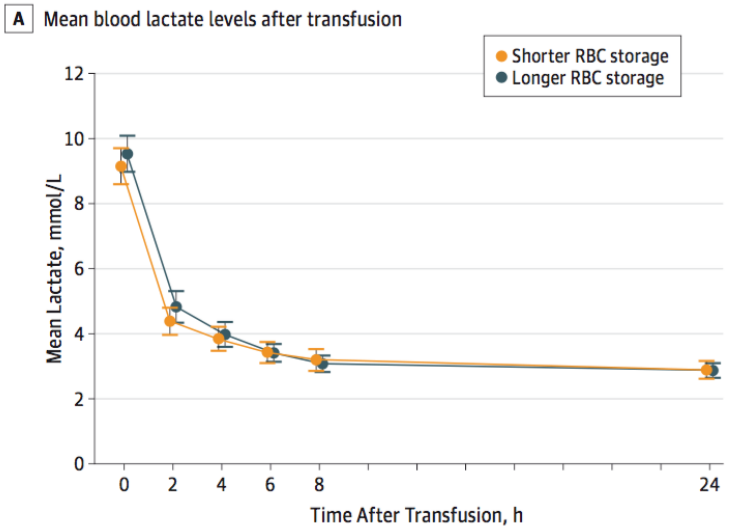
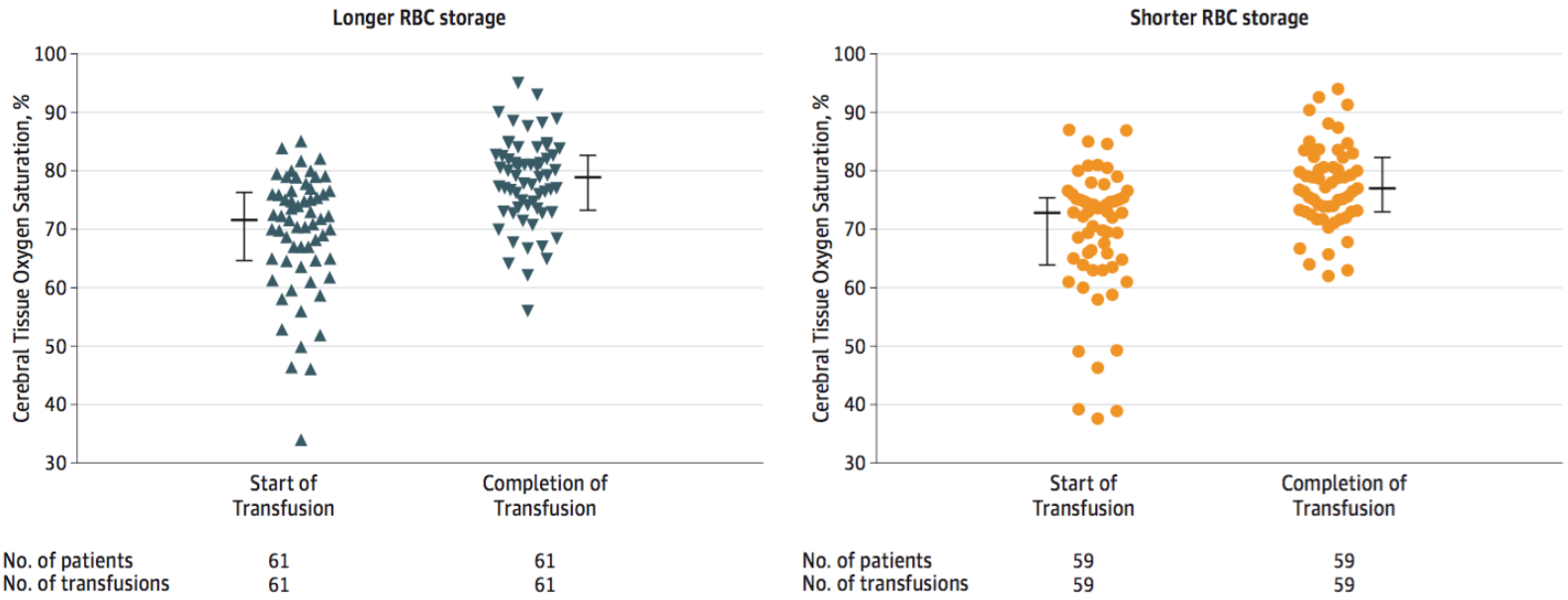


Figure 5. Cerebral Tissue Oxygen Saturation in Response to Transfusion

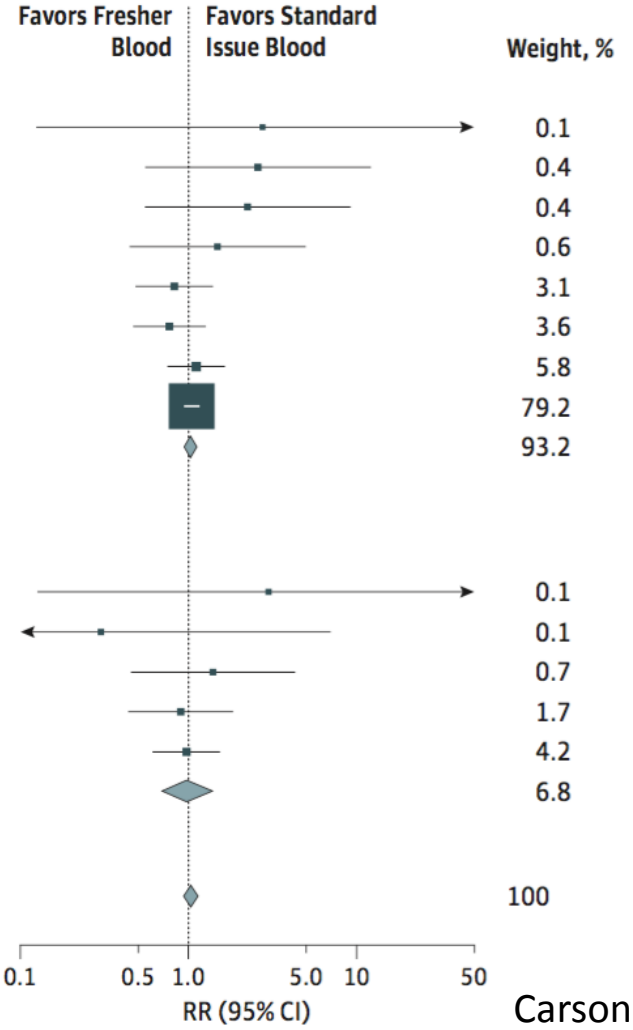


Dhabangi et al. *Lancet*. 2015

AABB Systematic Review-Storage Age

Figure 2. Association Between Fresher vs Standard-Issue Blood and Mortality in Adults, Neonates, Infants, and Children in Randomized Clinical Trials

Source	Fresher Blood: No. of Deaths	Fresher Blood: Total No.	Standard Issue Blood: No. of Deaths	Standard Issue Blood: Total No.	RR (95% CI)	Weight, %
Adults						
Bennett-Guerrero et al,[33] 2009	1	12	0	11	2.77 (0.12-61.65)	0.1
Aubron et al,[34] 2012	5	25	2	26	2.60 (0.55-12.19)	0.4
Schulman et al,[30] 2002	4	8	2	9	2.25 (0.55-9.17)	0.4
Hébert et al,[32] 2005	5	26	4	31	1.49 (0.45-4.98)	0.6
Steiner et al,[41] 2015	23	538	29	560	0.83 (0.48-1.41)	3.1
Kor et al,[37] 2012	17	50	22	50	0.77 (0.47-1.27)	3.6
Heddle et al,[36] 2012	35	309	61	601	1.12 (0.75-1.65)	5.8
Lacroix et al,[40] 2015	448	1211	430	1219	1.05 (0.94-1.17)	79.2
Subtotal	538	2179	550	2507	1.04 (0.95-1.15)	93.2
Heterogeneity: $\tau^2=0$; $\chi^2_7=5.47$; $P=.60$; $I^2=0\%$						
Tests for overall effect: z score = 0.85; $P=.40$						
Neonates, Infants, and Children						
Dhabangi et al,[38] 2013	1	37	0	37	3.00 (0.13-71.34)	0.1
Strauss et al,[29] 1996	0	21	1	19	0.30 (0.01-7.02)	0.1
Dhabangi et al,[39] 2015	7	143	5	143	1.40 (0.45-4.31)	0.7
Fernandes da Cunha et al,[31] 2005	9	26	10	26	0.90 (0.44-1.85)	1.7
Fergusson et al,[35] 2012	30	188	31	189	0.97 (0.61-1.54)	4.2
Subtotal	47	415	47	414	0.99 (0.69-1.42)	6.8
Heterogeneity: $\tau^2=0$; $\chi^2_4=1.46$; $P=.83$; $I^2=0\%$						
Tests for overall effect: z score = 0.06; $P=.96$						
Overall	585	2594	597	2921	1.04 (0.95-1.14)	100
Heterogeneity: $\tau^2=0$; $\chi^2_{12}=7.00$; $P=.86$; $I^2=0\%$						
Tests for overall effect: z score = 0.81; $P=.42$						
Tests for subgroup differences: $\chi^2_1=0.08$; $P=.78$; $I^2=0\%$						



Carson et al. *JAMA*. 2016

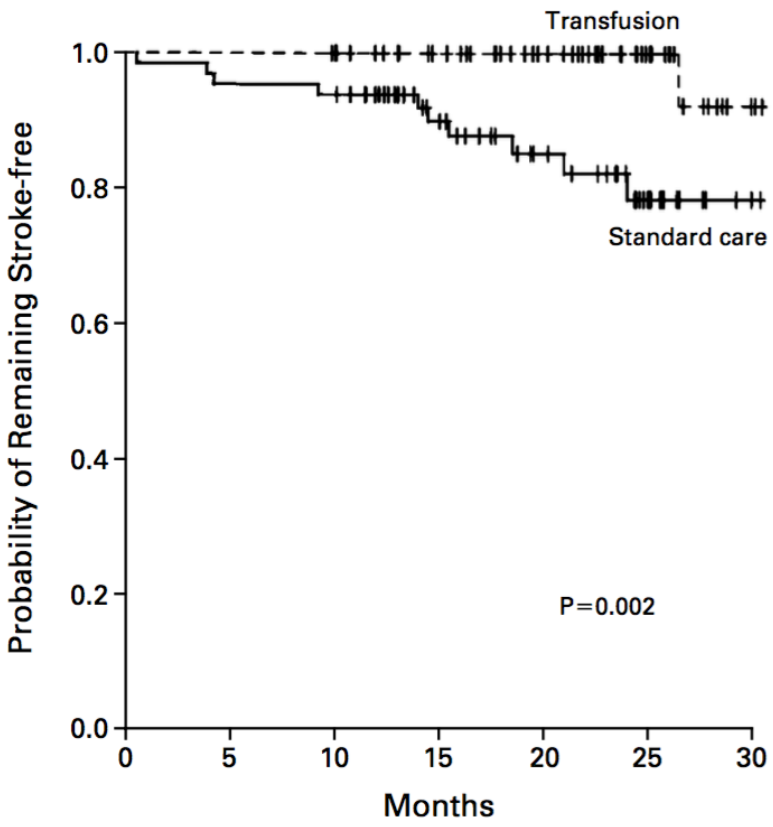
Age of RBC

- No clinical trial evidence to support using fresher blood

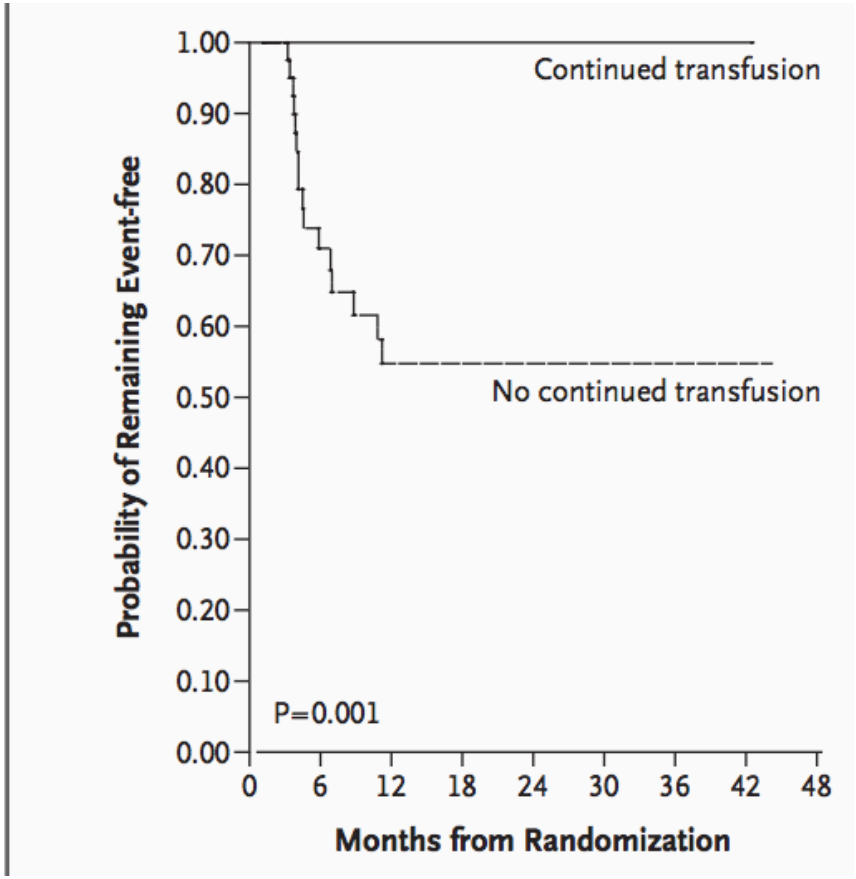
Outline

- Platelet Transfusion
  - Prophylactic threshold
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

STOP/STOP2: Prophylactic RBC Tx Prevents Stroke in SCD with high TCD



Adams et al. *NEJM*. 1998.



Adams et al. *NEJM*. 2005.

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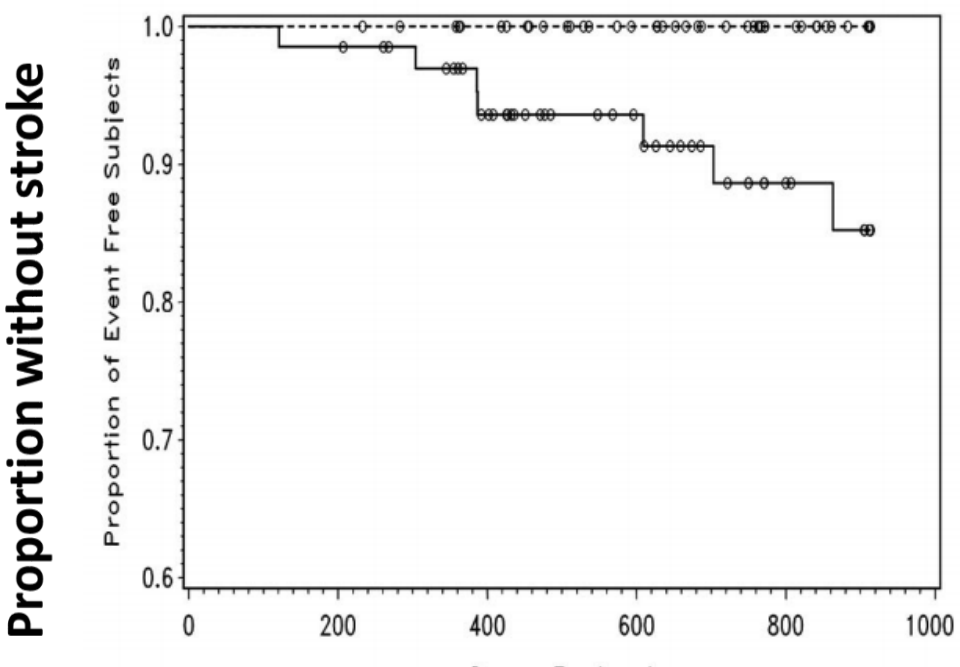
2˚ Stroke Prevention: Convert Tx to HU/Phlebotomy: SWITCH

- Non-inferiority RCT (n=134)
- Prior stroke, >1.5y tx, mean age 13y
- Composite endpoint: stroke and reduced LIC
- Terminated: LICs similar between groups



Ware et al. *Blood*. 2012

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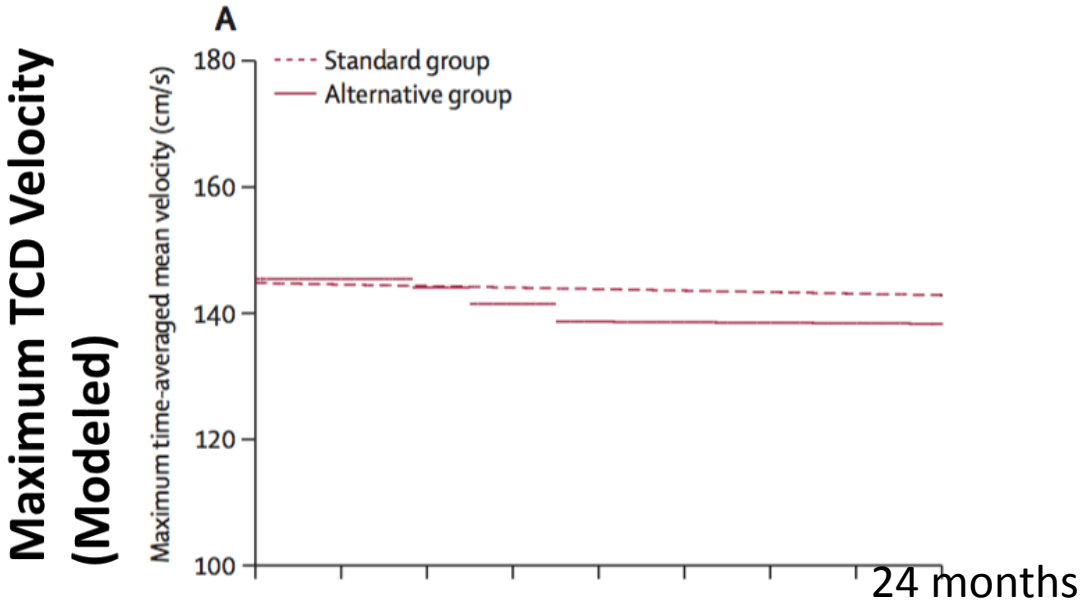
1˚ Stroke Prevention
Convert from Tx to HU: TWITCH

- Non-inferiority RCT
- 4-16y, TCD>200 cm/s, Tx>1y; no severe vasculopathy
- Primary outcome: change in TCD
- Terminated: non-inferiority demonstrated
- Avg HbF with HU: 27%



Ware et al. *Lancet*. 2016

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Silent Stroke (SCI) Prevention Transfusion (3y) vs. Std Care: SIT

- RCT, 5-15y, no stroke, SCI by MRI
- Primary outcome: stroke or new/larger SCI

	Transfusion (n=99)	No Transfusion (n=97)
Stroke (n)	**1**	**7**
New/Larger SCI (n)	**5**	**7**

- Also improvement in SCD morbidity (cf. SWITCH)
  - ACS, VOC, priapism, AVN, HA
- HU was exclusion
- Risk/benefit of iron loading

DeBaun et al. *NEJM*. 2015

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Pre-Op Tx is Important for SCD: TAPS Trial

- RCT of Tx vs. no Tx for low/moderate risk surgery (n=70)
- 97% HbSS, 60% <17y
- Terminated early: 30% (no Tx) vs. 3% (Tx) had SAE
  - Mostly ACS (n=9 vs n=1)

Howard et al. *Lancet*. 2013

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Summary: RBCs for SCD

- 2˚ stroke prevention: RBCs better than HU
- 1˚ stroke prevention: RBCs=HU
  - Aggressive HU
  - No severe vasculopathy
- SCI prevention: RBCs protect at-risk group from stroke
- Pre-operative RBCs important

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Outline

- Platelet Transfusion
  - Prophylactic threshold
- Red Cell Transfusion
  - Threshold for transfusion
  - Age of stored blood
  - SCD
- Granulocyte Transfusion

Granulocytes

- Indications
  - ANC <500 or qualitative defect
  - Bacterial/fungal infection not responsive to Abx
  - Chance for neutrophil recovery
- Must be ABO/Rh compatible (lots of RBCs)
- Irradiated
- CMV as appropriate
- Used ASAP <4h (?<6h after amphotericin)
- Donors get dexamethasone ± G-CSF
- Give blood bank notice if canceling granulocytes

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Evidence for Granulocyte Efficacy

- Best evidence from children (dose)
- No RCT
- Mean: 9 tx, $2x10^9$ granulocytes/kg
- 70% survival

Van de Wetering et al. *Eur J Cancer*. 2007.

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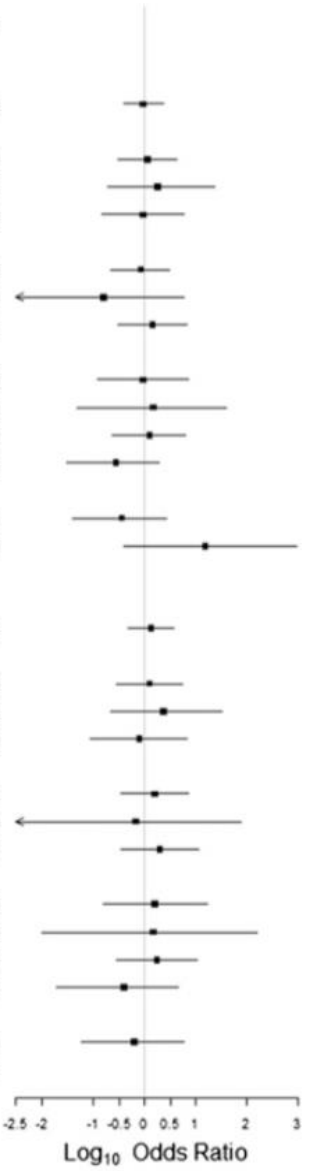
RING Trial

- Suspected bacterial/fungal infection with neutropenia (n=114)
- Primary outcome: alive and response to infection at 42 days
- 10% <18y

Price et al. *Blood.* 2015.

RING Trial- No differences

	Total N (% Success)	Granulocytes N (% Success)	Control N (% Success)	P-Value
MITT				
Overall	97 (42%)	48 (42%)	49 (43%)	>0.99
Bacterial Infection	51 (33%)	26 (35%)	25 (32%)	>0.99
Bacteremia Only	25 (24%)	14 (29%)	11 (18%)	0.66
Tissue Bacterial Infection	26 (42%)	12 (42%)	14 (43%)	>0.99
Fungal Infection	46 (52%)	22 (50%)	24 (54%)	>0.99
Fungemia Only	11 (64%)	3 (33%)	8 (75%)	0.49
Tissue Fungal Infection	35 (49%)	19 (53%)	16 (44%)	0.74
High Risk with Invasive Mold Infection	22 (55%)	13 (54%)	9 (56%)	>0.99
Low Risk with Invasive Mold Infection	9 (44%)	4 (50%)	5 (40%)	>0.99
High Risk with other Infection	41 (27%)	17 (29%)	24 (25%)	>0.99
Low Risk with other Infection	25 (56%)	14 (43%)	11 (73%)	0.23
Mold Pulmonary/Chest	23 (57%)	13 (46%)	10 (70%)	0.40
Mold ExtraPulmonary	10 (40%)	4 (75%)	6 (17%)	0.19
Per-Protocol				
Overall	74 (45%)	35 (49%)	39 (41%)	0.64
Bacterial Infection	38 (39%)	19 (42%)	19 (37%)	>0.99
Bacteremia Only	19 (32%)	10 (40%)	9 (22%)	0.63
Tissue Bacterial Infection	19 (47%)	9 (44%)	10 (50%)	>0.99
Fungal Infection	36 (50%)	16 (56%)	20 (45%)	0.74
Fungemia Only	7 (57%)	2 (50%)	5 (60%)	>0.99
Tissue Fungal Infection	29 (48%)	14 (57%)	15 (40%)	0.47
High Risk with Invasive Mold Infection	18 (61%)	9 (67%)	9 (56%)	>0.99
Low Risk with Invasive Mold Infection	7 (29%)	3 (33%)	4 (25%)	>0.99
High Risk with other Infection	32 (31%)	13 (38%)	19 (26%)	0.70
Low Risk with other Infection	17 (59%)	10 (50%)	7 (71%)	0.62
Mold Pulmonary/Chest	18 (61%)	9 (56%)	9 (67%)	>0.99
Mold ExtraPulmonary	8 (25%)	3 (67%)	5 (0%)	0.11



Price et al. *Blood.* 2015.

Limitations of RING Trial

- Terminated early: underpowered
- Patients receiving granulocytes are heterogeneous
  - E.g. Asymptomatic pulmonary fungal ball vs. skin necrosis from clostridium

Summary: Granulocyte Transfusion

- No high quality evidence for efficacy
- Still has role in select circumstances

Summary: So What Matters?

- Prophylactic platelet tx: minor difference
- Dose of platelets: no difference
- Threshold for RBC tx: no difference
- Age of stored blood: no difference
- SCD: RBCs=HU for 1˚ stroke prevention
- SCD: RBCs>HU for 2˚ stroke prevention
- SCD: RBCs superior for pre-op prophylaxis
- Granulocyte transfusion: no difference

Plasma…

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Future Studies in Peds Heme/Onc

- NHLBI Scientific Priorities in Transfusion Medicine (2016)
  - Coordination with trial groups to include transfusion data
  - Oncology/HSCT: Adjuncts to transfusion to prevent hemorrhage
    - Tranexamic acid, aminocaproic acid

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QUESTIONS?

Please type them in the chat box at the bottom left hand side of your screen.

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