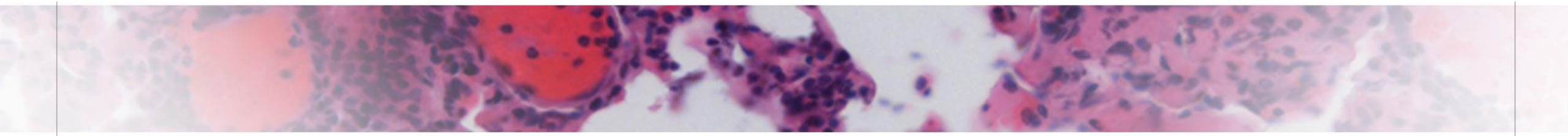


What is Patient Blood Management and where do we go from here?

Lawrence Tim Goodnough, MD
Professor Emeritus
Department of Pathology
Stanford University

Call to Reduce Transfusions:
National Summit on Overuse - September 2012

The Joint Commission
HELPING HEALTH CARE ORGANIZATIONS HELP PATIENTS

AMA
AMERICAN MEDICAL ASSOCIATION

"*Overuse/inappropriate use is defined as the use of a health service in circumstances where the likelihood of benefit is negligible or zero, and the patient is exposed to the risk of harm*."

Blood transfusion is one of five "overuse" interventions

How do we know that RBC Transfusions are over used?

Variation in Use of Blood Transfusion in Coronary Artery Bypass Graft Surgery

- STS database cohort of 82,446 patients undergoing primary isolated CABG surgery at 408 sites
- RBC (8% to 93%), plasma (0% to 98%), and platelet (0.4% to 90%) transfusions highly variable
- Three determinants: geographic location, academic status, and hospital volume

Variability in use, with no effect on patient outcomes, indicates inappropriate use of blood components in CABG.

Bennett-Guerrero E, et al. *JAMA* 2010;14:1568-1575.

Patient Blood Management

Period	I. Optimize Erythropoiesis	II. Minimize Blood Loss	III. Manage Anemia
Preoperative	Identify, evaluate, and treat underlying anemia Schedule preoperative autologous blood donation Consider erythropoiesis stimulating agent (ESA)	Identify and manage bleeding risk (past/family history) Review medications (antiplatelet, anticoagulation therapy) Minimize iatrogenic blood loss	Formulate patient-specific management plan using appropriate blood conservation modalities
Intraoperative	Schedule surgery after optimization of red blood cell mass is achieved	Employ meticulous hemostasis and surgical techniques Use acute normovolemic hemodilution (ANH) Utilize cell salvage/reinfusion Pharmacological/hemostatic agents	Optimize cardiac output Follow RESTRICTIVE, EVIDENCE-BASED TRANSFUSION STRATEGIES
Postoperative	IV iron, folate, ESA therapy if appropriate	Monitor and manage bleeding Use autologous blood salvage Minimize iatrogenic blood loss	Maximize oxygen delivery Follow RESTRICTIVE, EVIDENCE-BASED TRANSFUSION STRATEGIES

Modified, From Goodnough LT, Shander AS. Patient Blood Management. *Anesth* 2012;116: 1367-1376.
Goodnough LT, Marques M. Zika virus and patient blood management. *Anesth Analg* 2017; 124:282-9.

Practice Strategies for Elective Red Blood Cell Transfusion

- A traditional concept:

Blood transfusion is an effective therapeutic intervention

- A new paradigm:

Blood transfusion is an undesirable outcome

General Therapeutic Principles

1. Avoid an empiric, automatic transfusion threshold (for example, hemoglobin < 100 g/L [10g/dL]) [8.4]*
2. Regard elective transfusion with allogenic blood as an outcome to be avoided
3. **Administer transfusion on a unit-by-unit basis, according to symptoms. Remember: One unit of blood may be sufficient [8.4]***

*Reference: The case for the single transfusion.
J Garrott Allen NEJM 1972;19:984-85.
American College of Physicians
Audet AM, Goodnough LT. *Ann Int Med* 1992;116:403-406.
Welch HG, Meehan KR, Goodnough LT. *Ann Int Med* 1992;116:393-402.

Choosing Wisely®

An initiative of the ABIM Foundation

Ten Things Physicians and Patients Should Question

1 Don't transfuse more than the minimum number of red blood cell (RBC) units necessary to relieve symptoms of anemia or to return a patient to a safe hemoglobin range (7 to 8 g/dL in stable, non-cardiac in-patients).

Transfusion of the smallest effective dose of RBCs is recommended because liberal transfusion strategies do not improve outcomes when compared to restrictive strategies. Unnecessary transfusion generates costs and exposes patients to potential adverse effects without any likelihood of benefit. Clinicians are urged to avoid the routine administration of 2 units of RBCs if 1 unit is sufficient and to use appropriate weight-based dosing of RBCs in children.

Medical Society Guidelines/Recommendations for RBC Transfusions

Year	Society	Recommendations	Reference
1988	NIH Consensus Conference	7 g/dl (acute)*	JAMA 1988;260:2700
1992	Am Coll Physicians (ACP)	No number	Ann Int Med 1992;116:393-402
1996 2006	Amer Soc Anesth (ASA)	6 g/dl (acute)* No number	Anesth 1996;84:732-747 Anesth 2006;105:198-208
1997 1998	Can Med Assoc (CMA)	No number 6 g/dl (acute)*	Can Med Assoc J 1997;156:S1-S24 J Emerg Med 1998;16:129-31
1998	Coll Amer Path (CAP)	6 g/dl (acute)*	Arch Path Lab Med 1998;122:130-8
2001	Australasian Soc Blood Trans	7 g/dl	http://www.nhmrc.health.gov.au
2001 2012	Br Committee for Standards in Haematol	No number 7 g/dl (acute)* Unchanged	Br J Haematol 2001;113:24-3 http://www.bcshguidelines.com/documents/Admin_blood_components_bcsh_05012010.pdf

*Patients with acute blood loss
**Patients with ACS

Goodnough LT, Levy JH, Murphy MF. *Lancet* 2013;381:1845-54.

Medical Society Guidelines/Recommendations (Cont.)

Year	Society	Recommendations	Reference
2007 2011	Soc Thor Surg (STS) Soc Cardvasc Anesth (CVA)	7 g/dl or 8 g/dl (acute)*	Ann Thorac Surg 2007;83:S27-86 Ann Thorac Surg 2011;91:944-82
2011	SABM	8 g/dl	Trans Med Rev 2011;232-246
2012 2016	AABB AABB	7-8 g/dl or 8 g/dl** 7- g/dl or 8g/dl***	Ann Int Med 2012;157:49-58 Transfusion 2016;56:2627-2630.
2012	KDIGO****	No number	Kid Int 2012;2:311-316
2012	National Cancer Center Network (NCCN)	7 g/dl	JNCCN 2012;10:628-53
2016	UK Clinical Guidelines	7 g/dl (target 7-9) 8 g/dl (target 8-10)**	JAMA 2016;316:2039-9
2019	Frankfurt Consensus Conference	7-8 g/dL*****	JAMA 2019;321; 983-97

*For patients with acute blood loss
**For patients with symptoms of end organ ischemia
***For patients undergoing orthopaedic surgery and cardiac surgery; or cardiovascular risk factors
****Kidney Disease Improving Global Outcomes
***** Critical ill 7, cardiac surgery 7.5, hip fracture and cardiovascular disease 8, acute GI bleeding 7-8

Modified from Goodnough LT, Levy JH, Murphy MF. *Lancet* 2013;381:1845-54.

Eight Key Trials of RBC Transfusion in Adults

Clinical Setting (Ref)	Hemoglobin Threshold (g/dL)	Age (Years)	(%) Patients Transfused	(%) Deviation from Protocol	Mean Hemoglobin (g/dL)	Participation (%)
Intensive Care[1]	7 10	57.1 58.1	67 99	1.4 4.3	8.5 10.7	41
CT Surgery[2]	8 10	58.6 60.7	47 78	1.6 0.0	9.1 10.5	75
HipFx Repair[3]	8 10	81.5 81.8	41 97	9.0 5.6	7.9 9.2	56
Acute Upper GI Bleeding[4]	7 9	NA NA	49 86	9.0 3.0	7.3 8.0	93
Symptomatic CAD[5]	8 10	74.3 67.3	28.3 NA	1.8 9.1	7.9 9.3	12.2
Sepsis[6]	7 9	67 67	64 99	5.9 2.2.	7.7 9.3	82
TITR[7]	7.5 9	69.9 70.8	53.4 92.2	30 45	8-9 9.2-9.8	98
CT Surg[8]	7.5 9.5	72 72	52.3 72.6	NA NA	10 9	NA NA

1. Hebert PC. *NEJM* 1999;340:409.
2. Hajjar LA. *JAMA* 2010;304:1559.
3. Carson JL. *NEJM* 2011;365:2453.

Modified From Goodnough LT. *Am J Hematol* 2015;90:927-33.
Goodnough LT. *Med Clin N Amer* 2017;101:431-47.

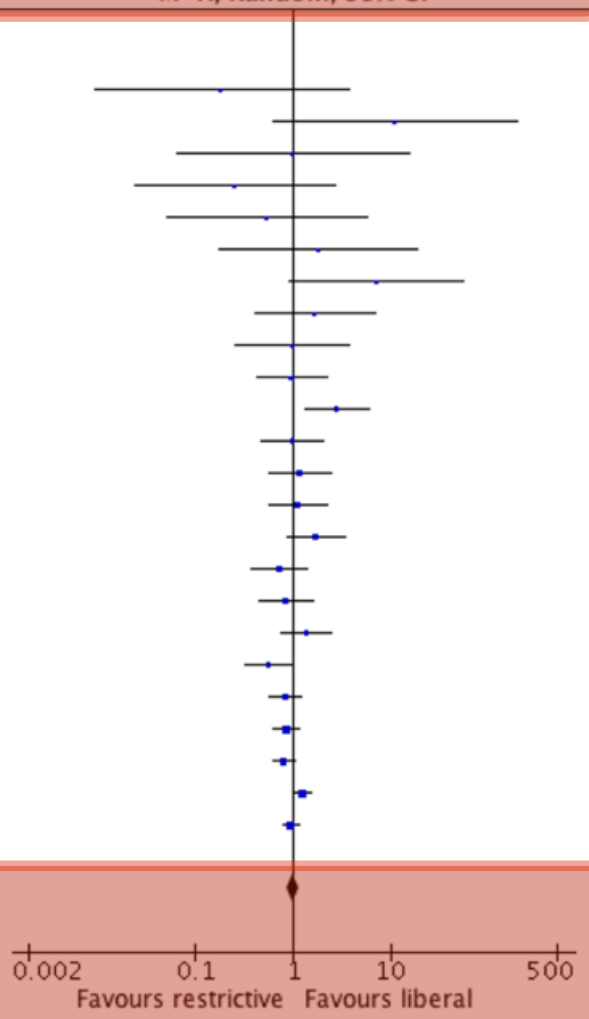
4. Villanueva C. *NEJM* 2013; 368:11.
5. Carson JL. *JAMA* Intern Med 2013;173:139.
6. Holst LB. *NEJM* 2014;371:1381.
7. Murphy GJ. *NEJM* 2015;372:997.
8. Mazer CD. *NEJM* 2017; 377:2133-2144.

Liberal vs Restrictive Trials: 30 Day Mortality

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
Laine 2017	0	40	0	40		Not estimable
Lotke 1999	0	62	0	65		Not estimable
Blair 1986	0	26	2	24	0.2%	0.19 [0.01, 3.67]
Foss 2009	5	60	0	60	0.3%	11.00 [0.62, 194.63]
Carson 1998	1	42	1	42	0.3%	1.00 [0.06, 15.47]
DeZern 2016	1	59	2	30	0.4%	0.25 [0.02, 2.69]
Webert 2008	1	29	2	31	0.4%	0.53 [0.05, 5.58]
Cooper 2011	2	23	1	21	0.4%	1.83 [0.18, 18.70]
Carson 2013	7	55	1	55	0.5%	7.00 [0.89, 55.01]
Parker 2013	5	100	3	100	1.1%	1.67 [0.41, 6.79]
Bush 1997	4	50	4	49	1.2%	0.98 [0.26, 3.70]
Hébert 1995	8	33	9	36	2.7%	0.97 [0.42, 2.22]
de Almeida 2015	23	101	8	97	3.2%	2.76 [1.30, 5.87]
Lacroix 2007	14	320	14	317	3.4%	0.99 [0.48, 2.04]
Hajjar 2010	15	249	13	253	3.4%	1.17 [0.57, 2.41]
Palmieri 2017	16	168	15	177	3.8%	1.12 [0.57, 2.20]
Gregersen 2015	21	144	12	140	3.9%	1.70 [0.87, 3.32]
Walsh 2013	12	51	16	49	4.2%	0.72 [0.38, 1.36]
Jairath 2015	14	257	25	382	4.2%	0.83 [0.44, 1.57]
Murphy 2015	26	1000	19	1003	4.7%	1.37 [0.76, 2.46]
Villanueva 2013	19	416	34	417	5.3%	0.56 [0.32, 0.97]
Carson 2011	43	1009	52	1007	7.9%	0.83 [0.56, 1.22]
Mazer 2017	74	2427	87	2429	10.2%	0.85 [0.63, 1.15]
Hébert 1999	78	418	98	420	11.4%	0.80 [0.61, 1.04]
Bergamin 2017	84	151	67	149	12.6%	1.24 [0.99, 1.55]
Holst 2014	168	502	175	496	14.4%	0.95 [0.80, 1.13]
Total (95% CI)		**7792**		**7889**	**100.0%**	**1.00 [0.86, 1.16]**
Total events	641		660			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 34.44$, df = 23 (P = 0.06); $I^2 = 33\%$

Test for overall effect: Z = 0.02 (P = 0.99)



Updated Cochrane Review: Carson Am Heart J 2018

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

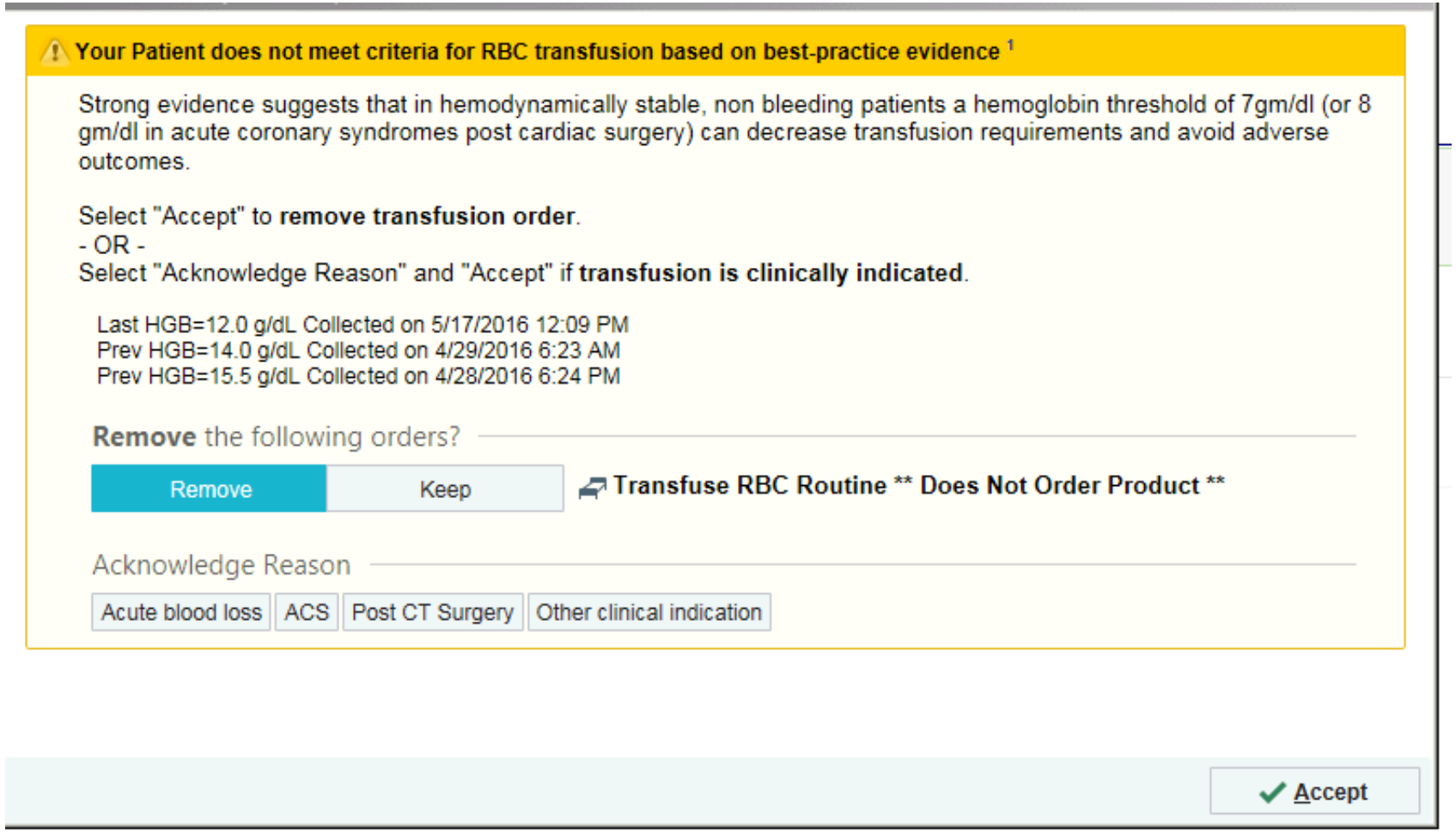
Indications for and Adverse Effects of Red-Cell Transfusion

Jeffrey L. Carson, M.D., Darrell J. Triulzi, M.D., and Paul M. Ness, M.D.

- Overall, the clinical trial data clearly show safety of restrictive transfusion threshold of 7-8 g/dL in most patients
- However, it is important to recognize that data from clinical trials is lacking in many subgroups
  - Acute coronary syndrome
  - Long-term dependence on transfusion
  - Pediatric patients
  - Acute neurological disorders

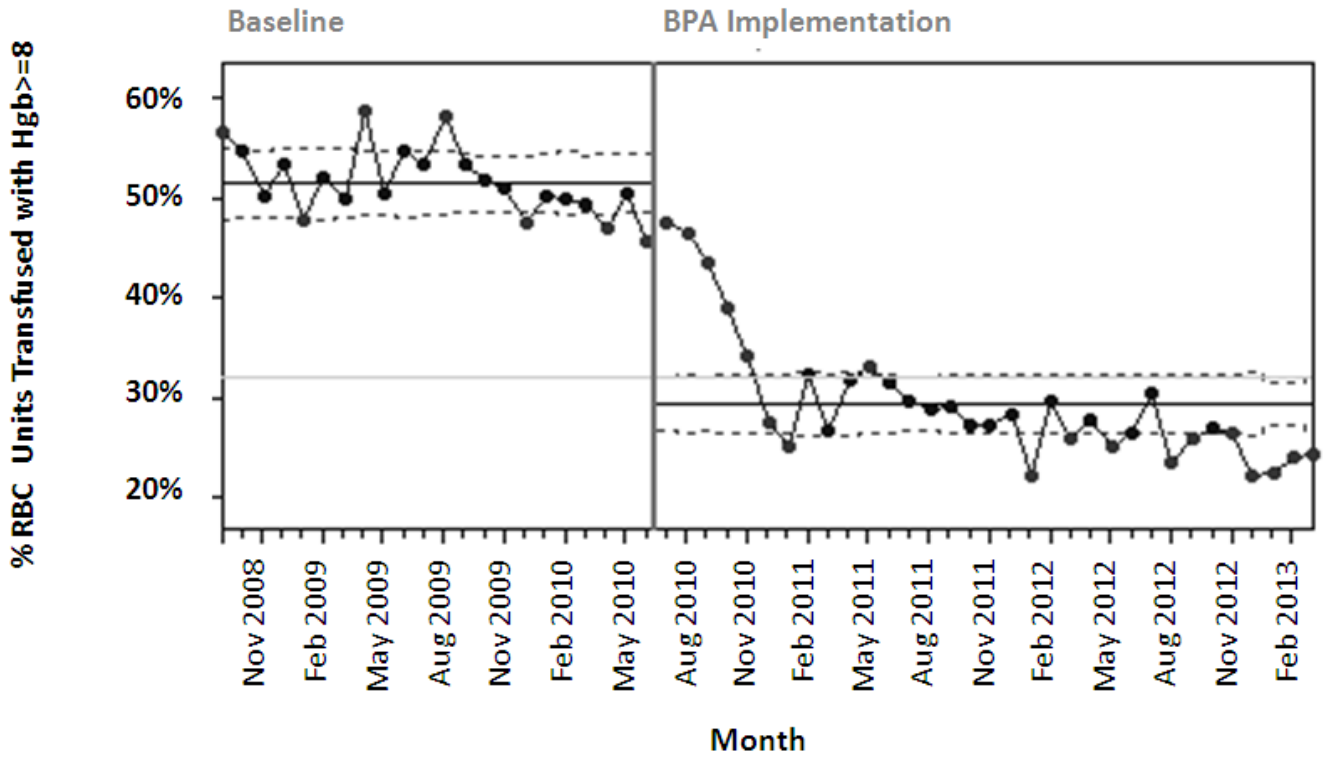
2017;377:1261-72.

Stanford Hospital & Clinics
Patient Blood Management Program
EPIC Best Practice Alert (BPA): Live July 2010



Updated from Goodnough et al. *Transfusion* 2014;54:1358-1365.

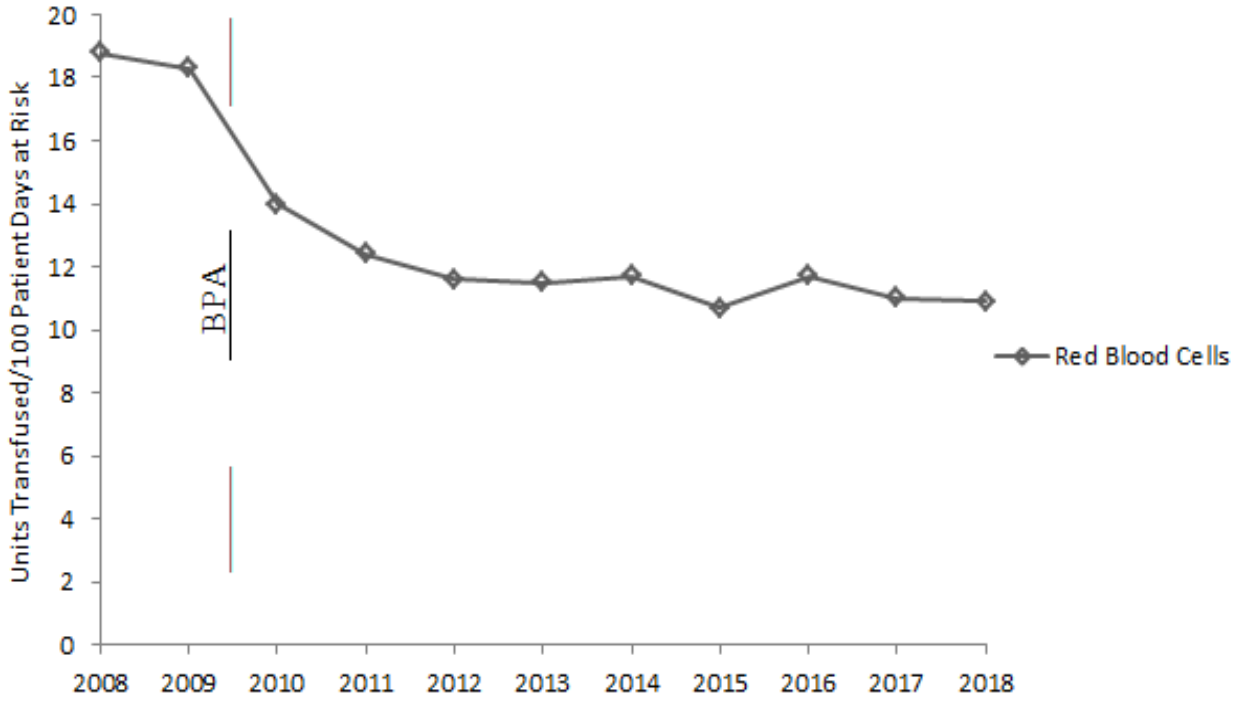
Blood Utilization



The percentage of stable patients transfused with RBC who last recorded hemoglobin was level > 8 gm/dL. From September 2008 through March 2013. Patients in procedural units (operating room, cardiac catheterization lab) were excluded, as were patients with a diagnosis of hemorrhage in the discharge problem list.

Goodnough LT, Shander AS. Patient Blood Management. Anesthesiology 2012;116:1367-76.

Trends in Blood Utilization at SHC, 2008-2018



Red blood cells issued, 2008-2018
BPA (best practice alert) implementation: July 2010
Abscissa numbers designate end of each year.

From: Goodnough LT, Hollenhorst MA. Clinical Decision Support and Improved Blood Utilization in Patient Blood Management. *Hematology* 2019 Dec 06;2019(1):577-582.

A 42% reduction in RBC utilization 2008-2015

Updated From: Goodnough LT, Baker S, Shah N. How do I use clinical decision support to improve red blood cell utilization. *Transfusion* 2016;56(10):2406-2411

Demographic Profile and Clinical Outcomes in Stable* Patients Transfused RBCs

Encounters	Pre-BPA**	Post-BPA*	p-value
n	3622	10528	
Age	59.7±17.4	59.8±17	0.76
% Female***	54.3	50.2	0.0001
Case Mix Index	2.78	2.86	0.0001
RBC Transfused	3.6±4.1	2.7±3.0	0.0001
LOS (days)	10.1±13.3	6.2±10.2	0.0001
% Mortality	5.5	3.3	0.0001
% 30 Day Readmission	13.7	8.5	0.0001
Discharge Hgb	9.9	9.0	0.0001

*Medical/surgical clinical units. Procedural areas (OR, Cath lab) excluded, also patients with discharge diagnoses/problem lists that include hemorrhage.

Pre-BPA, 21% of all patients at SHC were transfused.
Post-BPA, 17% of all patients at SHC were transfused.

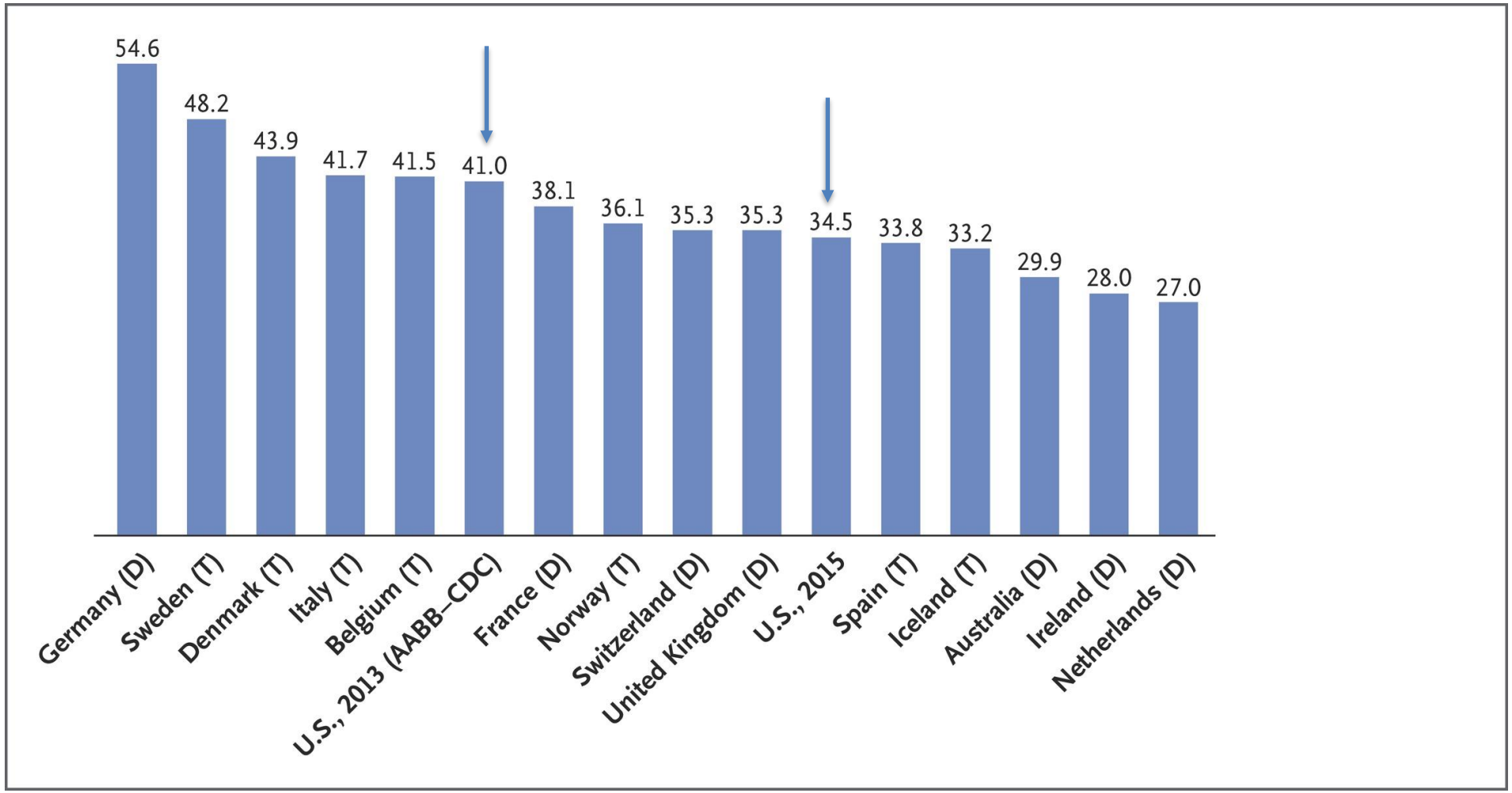
From Goodnough LT, et al. *Transfusion* 2014;54:1358-65.

Reduction of Transfusion

The hospital administrator directs you to reduce red blood cell transfusions in your center. Which of the following options might you propose

a. Implement a blood management program
b. Do not permit orders for daily blood work
c. Change orders for 2 units of RBC to 1 unit of RBC
d. Require a hematology consult for every patient
e. Tell the administrator that patients benefit from blood transfusion and it is not possible or appropriate to reduce red blood cell transfusion

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



Carson JL et al. *N Engl J Med* 2017;377:1261-1272.

Conclusion

1. A key component of Patient Blood Management is to improve blood utilization by promoting restrictive transfusion practices.

2. Clinical decision support can reduce inappropriate red blood cell transfusions .

3. Promotion of Patient Blood Management in the USA has had a profound impact on blood usage.

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Critical Care Societies Collaborative - **Critical Care**

1

Don’t order diagnostic tests at regular intervals (such as every day), but rather in response to specific clinical questions.

Many diagnostic studies (including chest radiographs, arterial blood gases, blood chemistries and counts and electrocardiograms) are ordered at regular intervals (e.g., daily). Compared with a practice of ordering tests only to help answer clinical questions, or when doing so will affect management, the routine ordering of tests increases health care costs, does not benefit patients and may in fact harm them. Potential harms include anemia due to unnecessary phlebotomy, which may necessitate risky and costly transfusion, and the aggressive work-up of incidental and non-pathological results found on routine studies.

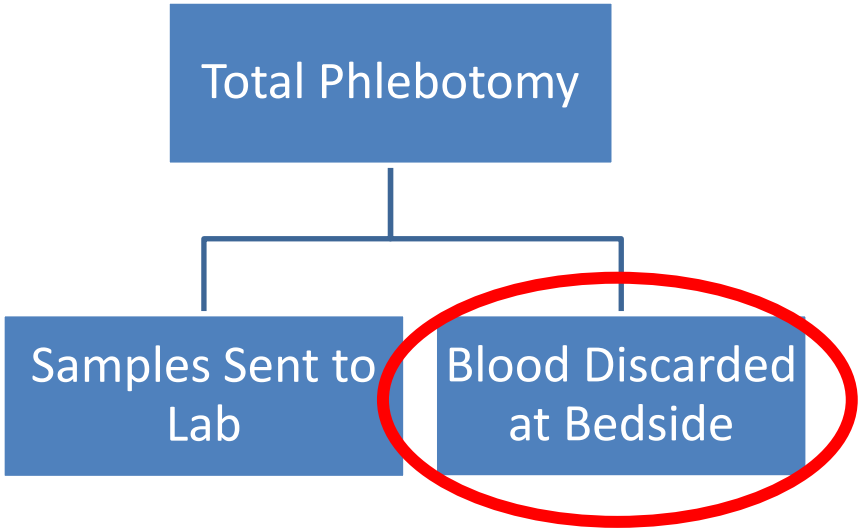
Study Objectives

1) Quantify average phlebotomy volume/pt-day, including blood waste, for patients in a tertiary care, academic medical/surgical ICU. Exclude patients with major bleeding.

2) Explore whether phlebotomy volume (ml/pt-day) is independently associated with:
   i. Anemia
   ii. Red blood cell transfusion
   iii. Mortality

Prospective Audit:
Waste Associated with ICU Phlebotomy

- Audit bedside phlebotomy
- Feb – Mar 2018
- Quantify waste per draw



Results and Conclusions

- Average waster was 14.8 ml per day from arterial line, PICC, and central line
- 63% had 3+ blood draws per day and 36% of patients had 5+ blood draws per day
- Every 10 mL increase in avg daily phlebotomy volume = OR 1.48 (95% CI 1.21 – 1.63) for nadir Hb < 80 g/L
- Every 10 mL increase in avg daily phlebotomy volume = OR 1.23 for RBC transfusion (95% CI 1.12 – 1.68)
- Every ml increased the odds of death by 1.03 (1.01-1.04)
  - Sickest patients get most blood tests

Plasma Case

- You are consulted by the Hospitalist service for a 58 year old male scheduled for needle biopsy of 2 cm retroperitoneal mass by interventional radiology.
- The patient has history of alcohol abuse, documented cirrhosis, and ejection fraction of 30%.
- INR is 1.8, and platelet count is 105,000
- Interventional radiology is insisting on administrating 2 units of plasma before the test.
- What do you recommend?

Plasma Case

1. Give 2 units of FFP as required by interventional radiology; need to get the procedure done
2. Refer radiologist to latest guidelines
3. Find a different radiologist to do the procedure or transfer the patient to a different hospital
4. Give 10-15 cc/Kg of Plasma before procedure and administer furosemide before and after the procedure
5. Only give plasma if the patient bleeds during/after the procedure

Identifying Inappropriate Use of Plasma Transfusion using a Novel Multicenter Electronic Data Audit*

Leigh Minuk[1] (MD), **Yang Liu**[2] (MMath), **Rebecca Barty**[2] (MLT, MSc), **Donald M. Arnold**[3] (MD, MSc), **Nancy M. Heddle**[3] (MSc), **Cyrus Hsia**[4] (MD), **Nadine Shehata**[5] (MD, MSc), **Ziad Solh**[6] (MD, MSc), **Troy Thompson**[7] (MLT BAHSc Hons.), **Alan Tinmouth**[8] (MD, MSc), **Robert Skeate**[9] (MD, MSc), **Jeannie Callum**[10] (MD)

[1]University of Toronto, Toronto, Ontario, Canada; [2]McMaster University, Hamilton, Ontario; [3]McMaster Centre for Transfusion Research, Hamilton, Ontario, Canada; [4]Division of Hematology, Western University, London, Ontario; [5]Mount Sinai Hospital, Toronto, Ontario; [6]Transfusion Medicine, Department of Pathology & Laboratory Medicine, Western University, London, Ontario, Canada; [7]Ontario Blood Regional Coordinating Network (ORBCoN), Sunnybrook Health Sciences Centre, Toronto, Ontario; [8]Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, Ontario; [9]Canadian Blood Services, Toronto, Ontario, Canada; [10]Department of Lab Medicine and Molecular Diagnostics, Sunnybrook Health Sciences Centre, Toronto, Ontario;

*3 Centers over one year period.

Sunnybrook HEALTH SCIENCES CENTRE

UNIVERSITY OF TORONTO

Criteria for inappropriate transfusions

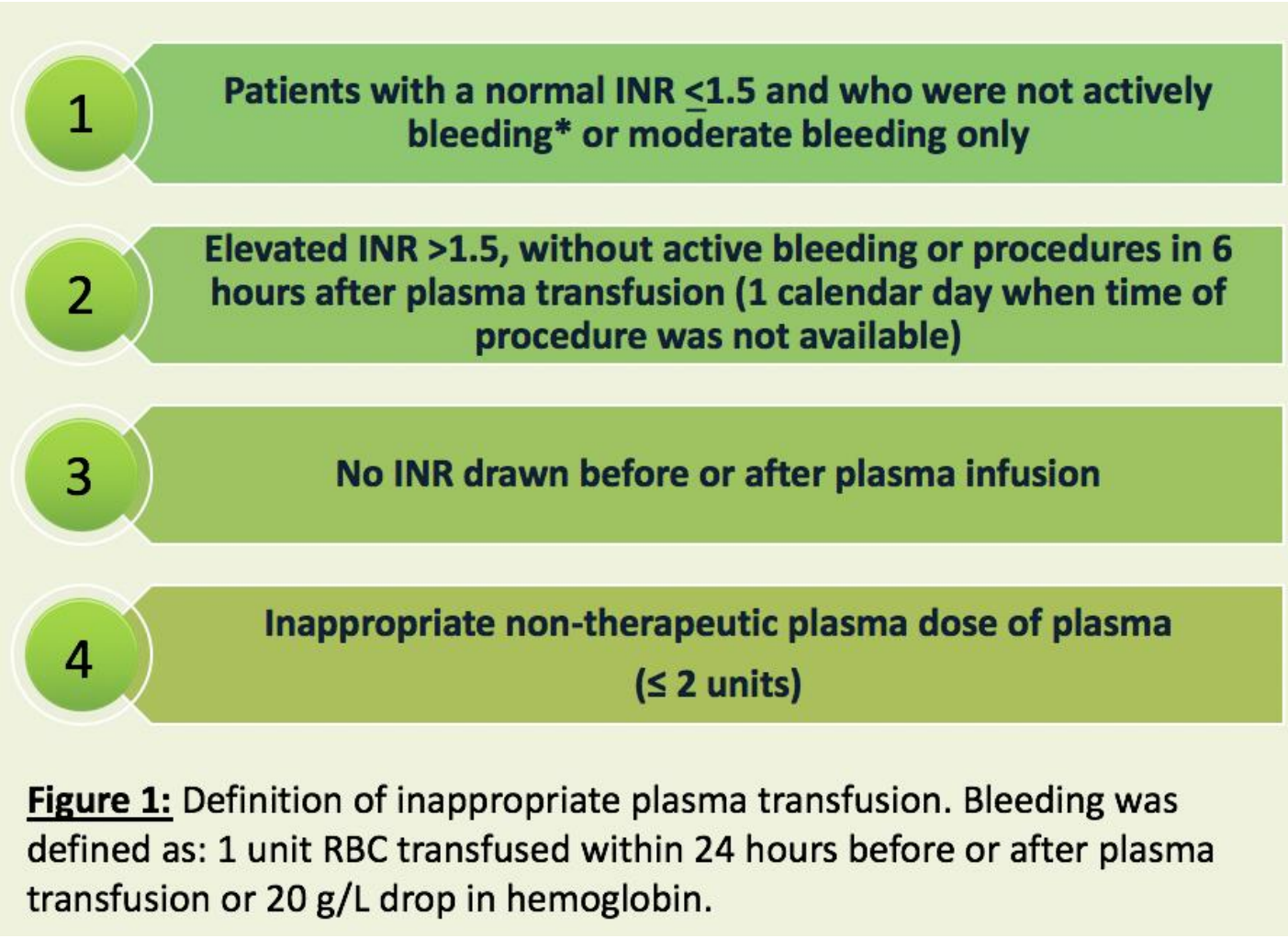


Figure 1: Definition of inappropriate plasma transfusion. Bleeding was defined as: 1 unit RBC transfused within 24 hours before or after plasma transfusion or 20 g/L drop in hemoglobin.

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>80% of Plasma was transfused inappropriately*

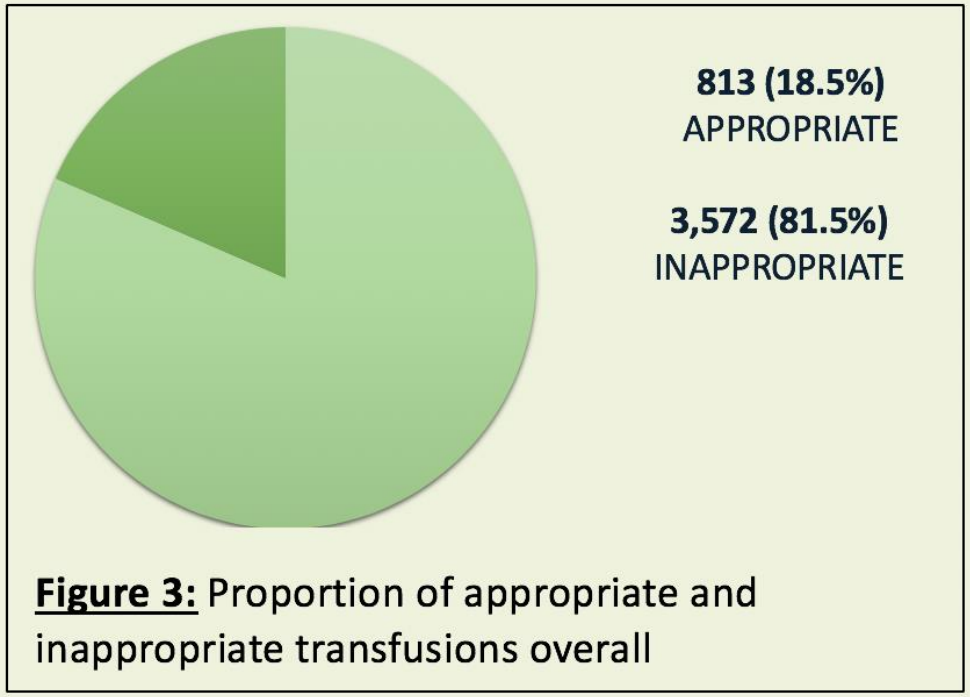

Figure 3: Proportion of appropriate and inappropriate transfusions overall

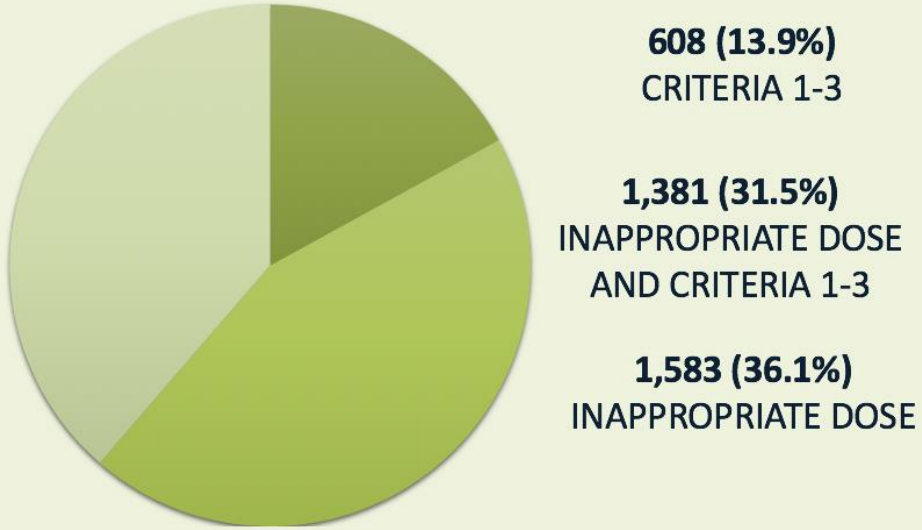

Figure 4: Categories of inappropriate transfusions as specified by criteria in Figure 1.

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*Leading to potential patient harm, unnecessary costs, and diversion of plasma away from a source for intravenous gamma globulin.

Plasma Case

1. Give 2 units of FFP as required by interventional radiology; need to get the procedure done
2. Refer radiologist to latest guidelines
3. Find a different radiologist to do the procedure or transfer the patient to a different hospital
4. Give 10-15 cc/Kg of FFP before procedure and administer furosemide before and after the procedure
5. Only give plasma if the patient bleeds during/after the procedure

! Your patient MAY NOT meet guidelines for platelet transfusion based on evidence. 1, 2

A platelet count of **20k** is sufficient for low risk procedures such as line placements, paracentesis, thoracentesis, and lumbar punctures.

A higher platelet count of 50k sould be trageted for higher risk procedures, surgeries, and on-going bleeding with 100k reserved for neurosurgery.

Antifibrinolytic agents should be considred to help control bleeding along with consultation with transfusion medicine (Pager # 12027) and hematology (SHC #27436 SCH/LPCH: #24362)

Last PLT, 9/21/2020 9:31 AM = 247k

Remove | Keep **Platelet Apheresis Product Order 9/22/202 6:00 AM**

Acknowledge Reason

Neurosurgery | CV surgery Bypass | ECMO | PLT function defect | CNS bleed | Other (commet)

ACCEPT

A RANDOMIZED STUDY OF A BPA FOR PLATELET TRANSFUSIONS

C Murphy, E Mau, E Pang, L Shieh, J Hom, N Shah

466 patients randomized to a visible vs nonvisible PPA alert group, used 25% fewer BPA eligible platelets, with mean monthly platelets 49 vs 66 for the control group(p=0.07) and platelets per inpt day at risk per month, 2.1 vs 2.4(p=0.53)

Patient Blood Management

Period	I. Optimize Erythropoiesis	II. Minimize Blood Loss	III. Manage Anemia
Preoperative	Identify, evaluate, and treat underlying anemia Schedule preoperative autologous blood donation Consider erythropoiesis stimulating agent (ESA)	Identify and manage bleeding risk (past/family history) Review medications (antiplatelet, anticoagulation therapy) Minimize iatrogenic blood loss	Formulate patient-specific management plan using appropriate blood conservation modalities
Intraoperative	Schedule surgery after optimization of red blood cell mass is achieved	Employ meticulous hemostasis and surgical techniques Use acute normovolemic hemodilution (ANH) Utilize cell salvage/reinfusion Pharmacological/hemostatic agents	Optimize cardiac output Follow RESTRICTIVE, EVIDENCE-BASED TRANSFUSION STRATEGIES
Postoperative	IV iron, folate, ESA therapy if appropriate	Monitor and manage bleeding Use autologous blood salvage Minimize iatrogenic blood loss	Maximize oxygen delivery Follow RESTRICTIVE, EVIDENCE-BASED TRANSFUSION STRATEGIES

Modified, From Goodnough LT, Shander AS. Patient Blood Management. *Anesth* 2012;116: 1367-1376.
Goodnough LT, Marques M. Zika virus and patient blood management. *Anesth Analg* 2017; 124:282-9.

BLOODLESS MEDICINE

CLINICAL CARE WITHOUT BLOOD TRANSFUSION

Jehovah’s Witnesses

Alloimmunized Patients

Autoimmune Hemolytic Anemias

Supply Constraints

Pandemics

War

Demographic Imbalances

CONCLUSIONS

- Patient Blood Management was initially promoted as Best Practices
- Clinical Decision Support is an effective tool for improving blood product utilization
- Outcome metrics from Institutional Quality Departments such as LOS, readmission rates, and mortality can be linked to blood product utilization
- Patient Blood Management has demonstrated that quality improvement(patient safety) reduces health care costs
- Patient Blood Management has now become a Standard of Care