Cardiac Blood Management Issues and Opportunities

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Cardiac Blood Management Issues

- Nationally ~20% of blood products are consumed by cardiac patients and CVS is typically the biggest user within a hospital
- Supply and demand for blood products remains tight and costs are still increasing
- Efficacy and safety issues for allogeneic transfusions (RBC, platelets, FFP) are becoming more clear
- Our cardiology colleagues keep "upping" the dose of anti-platelet agents
- In the past year, major controversies have surfaced surrounding pharmacologic therapies to reduce bleeding in cardiac patients
- External agencies (State, CMS, Payors) are requiring public reporting of outcomes
  - Will they also start looking at blood use?

Cardiac Blood Management Opportunities

- Blood utilization patterns are shifting from surgical to medical patients
- Improved utilization in high use specialties can yield substantial operational and financial benefits for hospitals and communities
- Of all surgical and medical specialties, cardiac surgery has done the most work to study effective blood management options
- Non-pharmacologic therapies continue to evolve, including surgical techniques, perfusion technologies, and point of care
- Complex healthcare scenarios can be substantially improved with multi-modal, multi-disciplinary approaches
- A systems approach to blood utilization would improve benchmarked outcomes such as LOS, morbidity, infections, mortality (through direct and indirect mechanisms)

What is Blood Management?

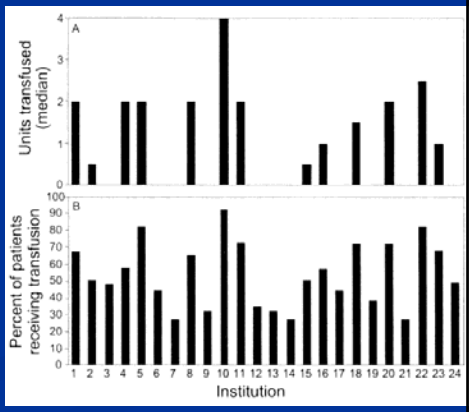
- **Blood management is a comprehensive, multidisciplinary process that is designed to promote the optimal use blood products throughout the hospital.**
- **The goal of blood management is ensure the safe and efficient use of the many resources involved in the complex process of blood component therapy.**

Is Blood Utilization Optimal?

Variation in Transfusion Practice- Cardiac Surgery

- Audit of transfusion practices for primary CABG patients at 24 U.S. institution
- Transfusion rates:
  - RBC 27- 92%
  - Platelets 0- 36%
  - FFP 0- 36%
  - Cryo 0- 17%

Why does this occur?



Stover et al, JCTVA 2000;14

Sources of Variation in Transfusion Practice

- Physician practice variation
  - Physicians make highly individualized trade-off decisions between the risks of anemia vs. the risks and benefits of transfusion
  - Several studies show this individualization is more aligned with the physician's bias rather than physiologic status of the patient
  - This decision is often based more upon custom and habit rather than formal training and current evidence based principles
- Institutional practice variation
  - Presence or absence of education, oversight and monitoring of blood utilization and blood management best practices

Transfusion "Trigger" Controversy

Transfusion trigger: "a particular hemoglobin level of discomfort in the prescribing physician, not defined by clear physiologic parameters" *-Spiess*

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

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

A multicenter, randomized controlled clinical trial of transfusion strategies in critical care

Hebert et al, NEJM 1999;340(6)

- Prospective, randomized multicenter Canadian study with 838 critically ill ICU patients
- Liberal transfusion strategy (Hb 10.0 g/dL) vs restrictive strategy (Hb 7.0 g/dL)
  - Restrictive transfusion group had a mean HgB of 8.5 and received 2.6 +/- 4.1 units
  - Liberal transfusion group mean HgB 10.7 and received 5.6 +/- 5.3 units

A multicenter, randomized controlled clinical trial of transfusion strategies in critical care

Hebert et al, NEJM 1999;340(6)

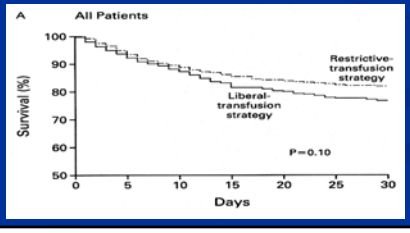
- **Overall, the adjusted multi-organ dysfunction score and in-hospital mortality were significantly higher in the *liberal* transfusion group than in the restrictive transfusion group**
- **No sub-group of these critically ill patients demonstrated an added benefit of higher Hgb levels, and most patients in the liberal transfusion group had worse outcomes.**

Hebert et al. Outcomes and Morbidity

	Restrictive (%)	Liberal (%)	P
MI	0.7	2.9	0.02*
Pulm edema	5.3	10.7	<0.01*
Angina	1.2	2.1	0.28
ARDS	7.7	11.4	0.06*
Infections	10.0	11.4	0.38

Hebert et al. Outcomes and Mortality at 30 days

	Restrictive (%)	Liberal (%)	p
All patients	18.7	23.3	0.10
APACHE ≤20	8.7	16.1	0.03*
<55yo	5.7	13.0	0.02*
Cardiac Dx	20.5	22.9	0.69
Death (Hosp)	22.2	28.1	0.05*



"A restrictive strategy of red cell transfusions is at least as effective as and possibly superior to a liberal strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction or unstable angina."

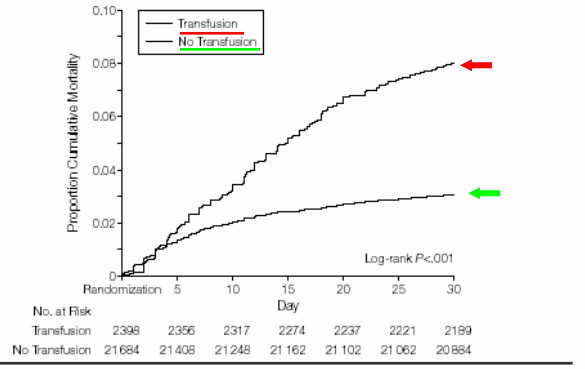
Hebert et al, NEJM 1999;340(6)

Relationship of blood transfusion and clinical outcomes in pts with ACS

Rao et al, JAMA 2004;292(13)

- Retrospective review of 24,112 patients with ACS from 3 large international trials (GUSTO IIb, PURSUIT, PARAGON B)
  - 10% of patients received a transfusion
- Extensive database of patient variables, outcomes data, and resource utilization from prospective, randomized trials of ACS interventions
- Multivariate analysis + propensity scoring to adjust for confounding factors predicting adverse outcomes and mortality (5 different statistical models)
  - age, race, weight, diabetes, BP, HR, onset time of symp., stroke, MI, sex, angina, HTN., hyperlipidemia, Fm. Hx. CAD,CHF, peripheral vascular dx, PCI, CABG, Killip class, baseline Hct., max creatinine at baseline, chronic renal insufficiency, ST-segment elevation, Beta blocker use, calcium channel blocker use, nitrate use, smoking

Figure 1. Kaplan-Meier Estimates of 30-Day Mortality Among Patients Who Did and Did Not Receive Blood Transfusion



Rao et al, JAMA 2004;292(13)
Unadjusted data

Relationship of blood transfusion and clinical outcomes in pts with ACS

Rao et al, JAMA 2004;292(13)

- Adjusted probability of mortality with transfusion as an independent predictor was OR 3.94
- Landmark analysis (ala Wu, NEJM 1999) showed predicted probability of 30 day mortality increased with transfusion above HCT 25%

Adjusted data

Table 4. Adjusted Predicted Probabilities of 30-Day Death With and Without Transfusion by Nadir Hematocrit Value

	Nadir Hematocrit, %*			
	20	25	30	35
Adjusted odds ratio (95% CI)†	1.59 (0.95-2.66)	1.13 (0.70-1.82)	168.64 (7.49-3797.69)	291.64 (10.28-8273.85)

Abbreviation: CI, confidence interval.

"Blood transfusion in the setting of acute coronary syndromes is associated with higher mortality, and this association persists after adjustment for other predictive factors and timing of events."

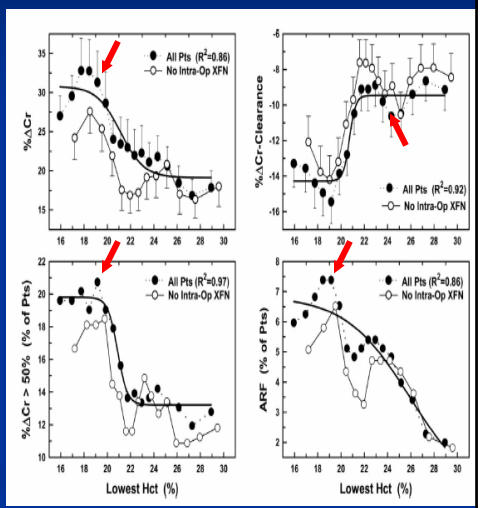
"We suggest caution regarding the routine use of blood transfusion to maintain arbitrary hematocrit levels in stable patients with ischemic heart disease."

Rao et al, JAMA 2004;292(13)

Role of hemodilutional anemia and transfusion during CPB in renal injury after CABG

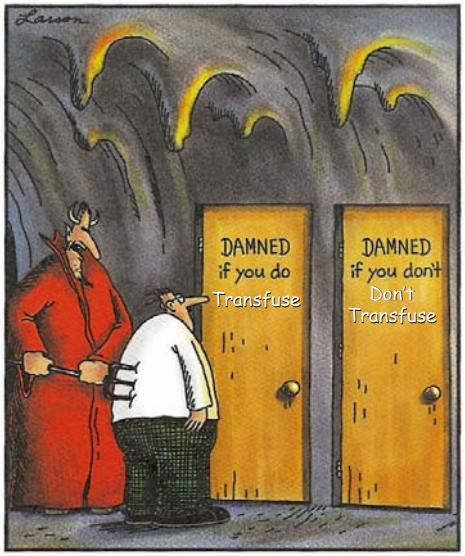
-Habib, CritCareMed 2005;33(8)

- Retrospective review of 1760 CABG patients circa 2002-2004
- Impact of nadir HCT, CPB time and transfusion on renal dysfcn using mulitvariate analysis and propensity score
- Nadir HCT <24% assoc with renal dysfcn and ARF
- Transfusion *increased* renal injury at HCT < 24%
  - Renal inj 14.4% -> 26.0%
  - ARF 3.4% -> 12.0%
  - LOS 6.3d -> 8.1d
  - Mortality 1.4% -> 3.8%



"This need (to test the efficacy of methods aimed at minimizing CPB hemodilution) is amplified by growing evidence, including from this study, of the adverse effects and ineffectiveness of packed RBC transfusions as a means to avoid excessive hemodilutional anemia."

-Habib, CritCareMed 2005;33(8)



"C'mon, c'mon—it's either one or the other."

-Spiess, CritCareMed 2005;33(8)

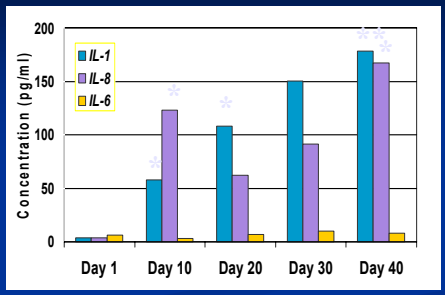
Why Don't Transfusions Seem to Improve Outcomes in Anemic Patients?

Stored allogeneic blood is an imperfect substitute for endogenous hemoglobin!

- Ineffective Exchange
  - Impaired tissue oxygen delivery due to storage defects
- Excess Baggage
  - Adverse effects and immune system changes as a consequence of allogeneic transplantation

Storage Defects and Microvascular Perfusion

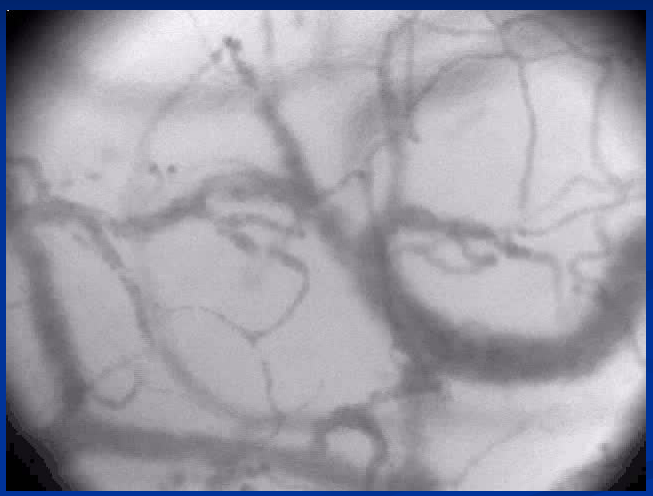
- Decreased 2,3- DPG, ADP
- Build-up of cytokines, free Hgb, K+, debris (BRMs)
- Poor deformability



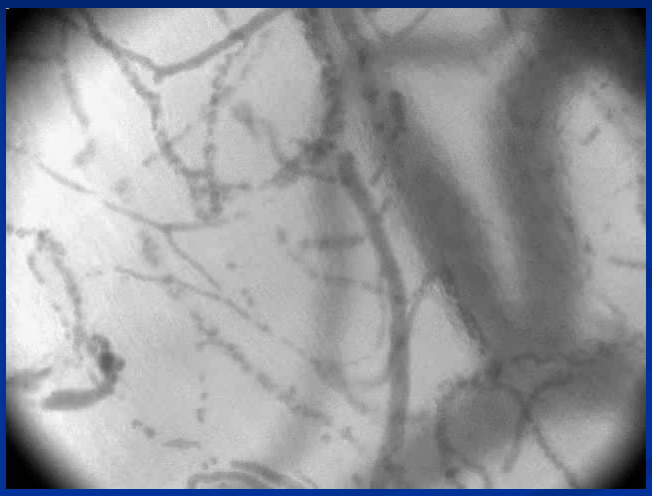
Kristiansson, Acta Anesth Scand 1996; 40

Hovav, Transfusion 1999;39

Transfusion and Microcirculatory Dynamics- Cytoscan Pre-Transfusion

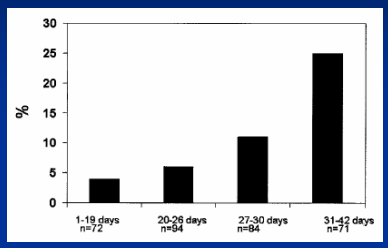


Cytoscan Post-Transfusion

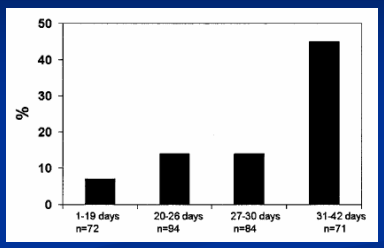


The Association Between Duration of RBC Storage and Morbidity and Mortality After Reop CABG

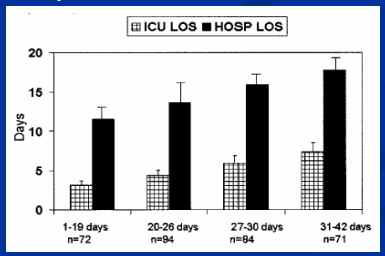
Basran et al, Anesth Analg 2006;103



In Hospital Mortality



ARF



LOS

Adverse Effects of Allogeneic Transplantation

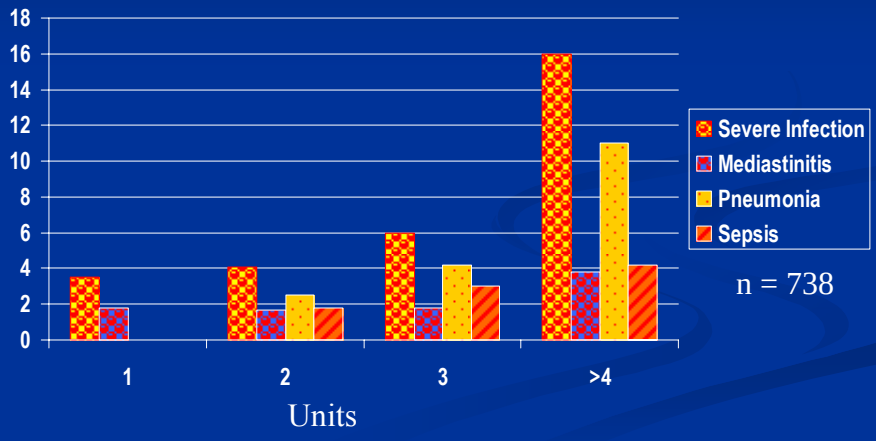
- Infectious Complications
  - Viral, bacterial contamination of platelets* (1:3000), other (nvCJD, West Nile, Chagas)
- Febrile and allergic reactions
- Hemolytic transfusion reactions* (clerical)
  - Leading cause of morbidity and mortality
- Other
  - Microchimerism (50%/ 15%), GVHD
  - SIRS, TACO, TRALI*

Transfusion Related Immunomodulation (TRIM)

Allogeneic transfusions cause dose- dependent alterations in immune system function

- Upregulation of humoral immunity
- Decreases in NK cell and macrophage activity, activation of T-suppressor cells (anergy)
- Effect has been known and well-documented for years

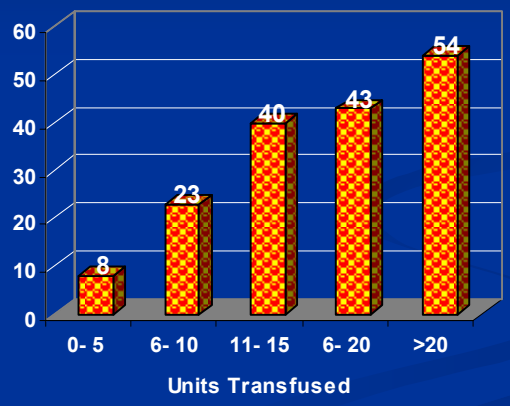
Dose-Response for Transfusion and Infection in Cardiac Surgery



n = 738

Leal-Noval et al. Chest 2001;119

Dose Response for Post-injury Multiple Organ Failure

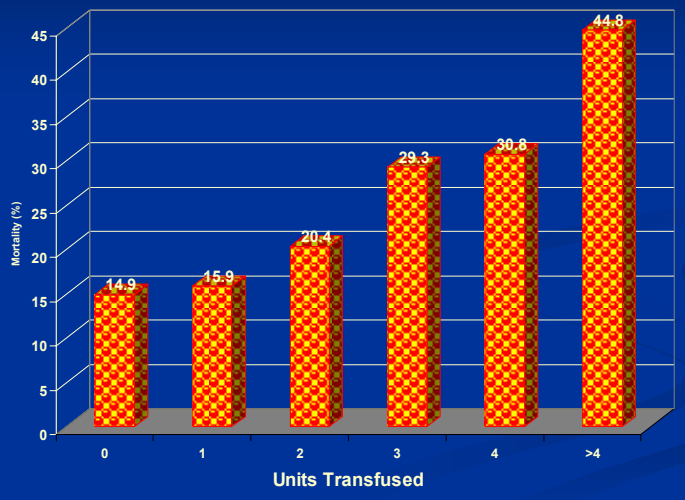


MOF(%)

OR 7.4- 13.2
n = 513

Moore et al, Arch Surg 1997;(132)

Dose Response for Mortality and Transfusion in Critical Care



OR 1.4

n= 1136

Vincent et al, JAMA 2002; 288(12)

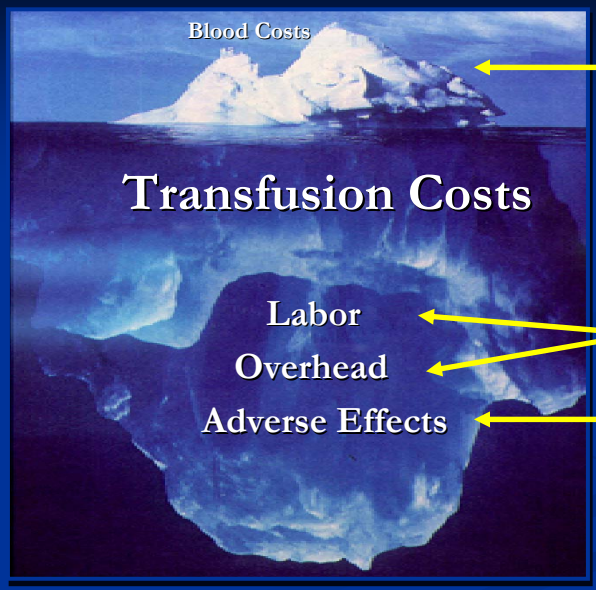
Dose Response for Length of Stay in Critical Care

n = 576

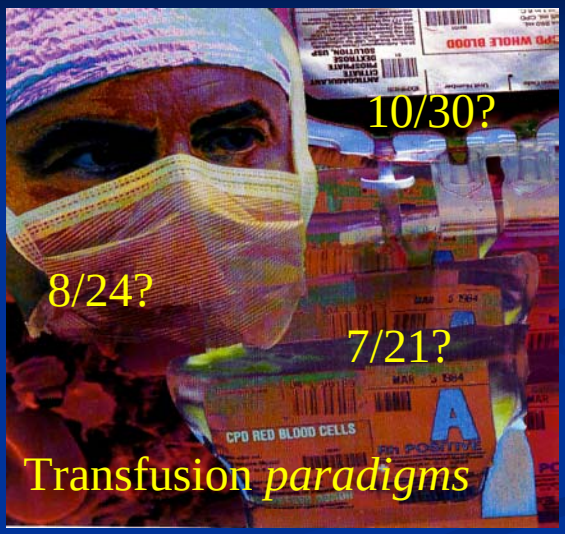
Shapiro et al, J Trauma 2003;55

Hospital Resource Variable Costs

Hospital Resource	Variable Cost (2004$)
Operating room variable time	$1730- $2880/ hour
Postoperative hospital day	$1200/ day
ICU day	$3400/ day
ICU day- ventilated patient	$4400/ day
Ventilator-associated pneumonia	$15,500
Serious postoperative infection- orthopedic surgery patient	17,500- $18,800
Postoperative deep sternal infection- cardiac surgery patient	$25,600
Post procedure bleeding- Percutaneous Coronary Intervention	$13,700
Reoperation for bleeding- cardiac surgery patient	$26,900- $28,600
*Red blood cell transfusion- variable cost per unit	$1700- $2500/ unit



Transfusion "Trigger" Controversy



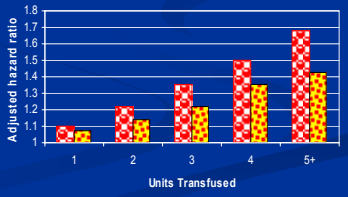
STRATEGIC BLOOD MANAGEMENT

Applied Blood Management

Blood is still the best thing possible to have in our veins…

Maintain RCM!

- Ensure that every unit of blood transfused is appropriate
  - Minimize transfusion, complications and anemia
  - Efficient use of all resources (drugs, devices)
- Organizational principles
  - Attention to detail
  - Multidisciplinary approach
  - Utilization of evidence-based guidelines and clinical best practices
  - Reduce risk exposure
  - Proactive patient management systems



- **USE THIS FORM FOR ALL BLOOD COMPONENT TRANSFUSION ORDERS.**
- **Check off at least one indication for each type of blood component order.**
- **The minimal effective dose of all blood components should be used; SINGLE UNIT transfusions of red cells are often effective.**
- **Compliance with transfusion guidelines will be monitored by the transfusion committee.**
- **The blood bank phone # is 803-0421 (86th Strret).**

❑ **Blood Transfusion Consent signed**
TRANSFUSION ORDER (indicate type and amount):_____
Request for special red cell products: _____ Irradiated _____ Washed _____ CMV negative
Patient location (3E, ICU, OR, PACU, etc)_____ Utilization review❑
INDICATION (check all that apply):
Packed Red Cells **Most recent hemoglobin _____g/dL or hematocrit_____%**
One unit of packed red cells in an adult, 8 mL/kg pediatric dose, will increase hematocrit by approximately 3% and hemoglobin by 1 g/dL.
❑ Hematocrit ≤ 21% or hemoglobin ≤ 7 g/dL.
❑ Hematocrit ≤ 24% or hemoglobin ≤ 8g/dL in a patient with coronary artery disease and unstable angina/ myocardial infarction/ cardiogenic shock
❑ Rapid blood loss with > 30- 40% of estimated blood volume (>1500- 2000 mL) not responding to appropriate volume resuscitation, or with ongoing blood loss.
❑ The patient has been determined to be normovolemic and there is evidence to support the need for increased oxygen carrying capacity as witnessed by (indicate):
NOTE: ***these indications will be tracked and may be peer reviewed***
❑ Tachycardia, hypotension not corrected by adequate volume replacement alone
❑ PVO_2 < 25 torr, extraction ratio > 50%, VO_2 < 50% of baseline - *specify*_____
❑ Other- *specify*_____
❑ Autologous predonate red cells: same as allogeniev

Platelets **Most recent platelet count _____/ cc^3**
A single dose of platelets (adult: one apheresis or 6 concentrates; pediatric dose 1 unit/10 kg) will increase the platelet count by 25,000- 35,000/ cc^3
❑ Platelet count ≤ 10,000/ cc^3 prophylactically in a patient with failure of platelet production
❑ Platelet count ≤ 20,000/ cc^3 and signs of hemorrhagic diasthesis (petechiae, mucosal bleeding)
❑ Platelet count ≤ 50,000/ cc^3 in a patient with (indicate):
❑ Active hemorrhage
❑ Invasive procedure (recent, in-progress, planned)
❑ Platelet dysfunction as documented by- *specify*_____

Fresh Frozen Plasma **Most recent coag. studies: PT___ INR ___ PTT ___ Fibrinogen _____**
A dose of 10- 15 mL/ kg is usually adequate to correct a coagulopathy. **Patient weight _____ kg**
❑ Abnormal coagulation studies and significant hemorrhage
❑ Prophylactic use for PT/ APTT > 1.5 times the mean of the reference range
❑ Emergent reversal of coumadin

Cryoprecipitate **Most recent coag. studies: PT___ INR ___ PTT ___ Fibrinogen _____**
One unit per 10 kg is usually adequate when cryoprecipitate is required. **Patient weight _____ kg**
❑ Fibrinogen ≤ 100 mg/ dL
❑ Fibrinogen ≤ 150 mg/dL with active hemorrhage

_____/_____ _____ _____ _____
Physician's signature / printed name Pager # Date Time

Trust…
but verify.
-Ronald Reagan

Speak softly…
and carry a big stick.
-Theodore Roosevelt

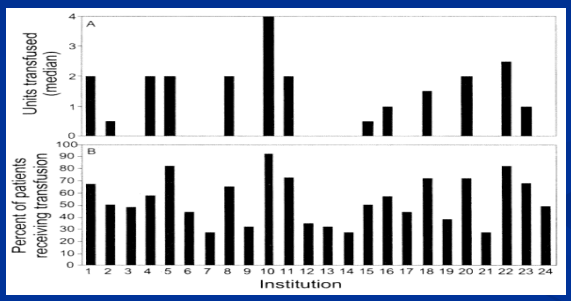
Multidisciplinary Teams- Cardiac Surgery

- Cardiac surgeons
- Anesthesiologists
- Perfusion
- Nurses- CR/ CVPV
- Physician's Assistants
- Pharmacists
- Laboratory/ Blood Bank
- Administrative support
  - Supervisory
  - Purchasing
  - Quality
  - Financial

21 Cardiac Blood Management Opportunities

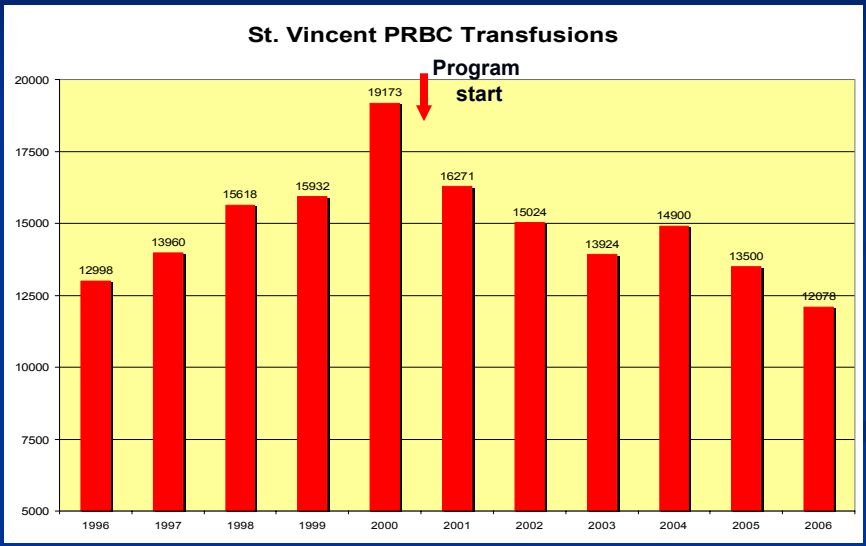
- **Preoperative**
  - Risk stratification and intervention
  - Anemia management
  - Iatrogenic blood loss (during cardiac catheterization)
  - Cessation of drugs that increase bleeding
- **Intraoperative**
  - Avoidance of hemodilution
  - Heparin management protocols
  - Pump prime volumes
  - Pump circuit coatings
  - Perfusion techniques
  - Autotransfusion techniques
- **Intraoperative (cont)**
  - Surgical techniques
  - Anesthetic techniques
  - Pharmacologic therapies
  - Topical hemostatic agents
  - Point of care testing
    - Hemoglobin
    - Coagulation status
  - Coagulation management protocols
  - Rewarming protocols
- **Postoperative**
  - Point of care testing
  - Postoperative autotransfusion
  - Iatrogenic blood loss
  - Evidence-based guidelines

Variation in transfusion rates among institutions is the end result of the actions or inactions of organizations to manage the series of events that ultimately lead to blood transfusions.

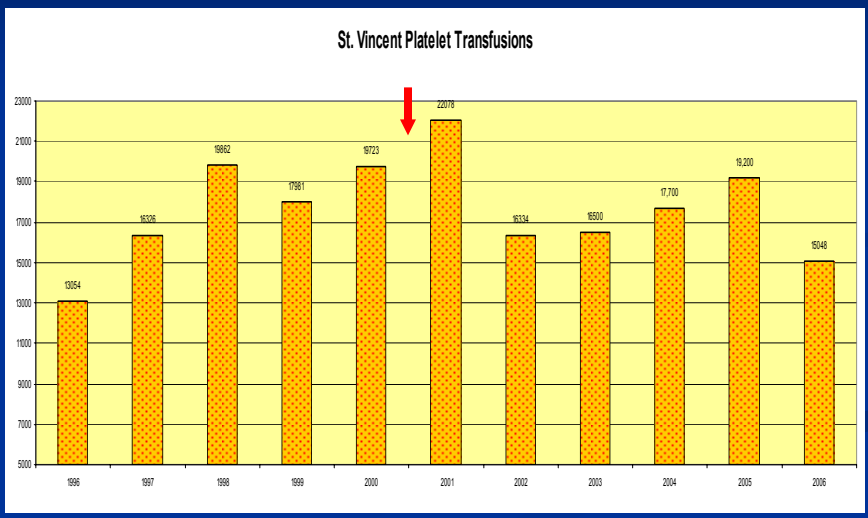


Further, this series of events is largely predictable and to a great extent is controllable.

37% Reduction in Red Blood Cell Transfusions



32% Reduction in Total Platelet Transfusions



Blood Management Program Cost Savings- Red Blood Cells

	Program Annual Savings	Program Lifetime Savings
Reduction in RBC transfusions (average)	**3800 units**	**22,800 units**
Blood acquisition cost savings*	**$800,000**	**$4,800,000**
Transfusion cost savings	**$2,200,000**	**$13,200,000**
Reduction in adverse events	**$4,600,000**	**$27,600,000**
Total hospital cost savings*	***$7,600,000***	***$45,600,000***

*RBC acquisition cost $210/ unit
**Platelet total cost savings add $1.9M annual/ $11.4M lifetime