


# RESTRICTIVE VS LIBERAL TRANSFUSION STRATEGIES



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October 19, 2018

# Disclosure, Attestation, & Content Validation

- ▣ No financial relationship with any commercial interest
- ▣ I understand all the recommendations involving clinical medicine in a CME activity must be based on evidence that is accepted within the profession of medicine as adequate justifications for their indication and contraindications in the care of patients

# Objectives

- ▣ Discuss the importance of optimization of oxygen delivery during shock
- ▣ Discuss critically ill patient populations that would benefit from restrictive vs liberal transfusion strategies

# Oxygen Requirement Various Tissues

- ▣ Each organ system in body has different oxygen requirement that must be met to maintain normal homeostasis
- ▣ Adequate tissue oxygenation is determined by the balance between the oxygen delivered and the oxygen required to sustain aerobic metabolism

# Oxygen Utilization

- ▣ The most efficient means of generating ATP is through oxidative phosphorylation, in which oxygen serves as terminal electron acceptor
- ▣ Aerobic metabolism
  - 36 ATP
  - H<sub>2</sub>O
- ▣ Anaerobic metabolism
  - 2 ATP
  - Lactate

# Shock

- ▣ Pathologic condition when oxygen supply becomes the rate-limiting step in the generation of energy; a condition of hypoperfusion at a cellular level when oxygen delivery ( $DO_2$ ) to the cells is below the tissue oxygen consumption ( $VO_2$ )



# Oxygen Content

- ▣ Oxygen content
  - $CaO_2 = (1.34 \text{ Hb} \times SaO_2) + (PaO_2 \times 0.003)$ 
    - ▣ Hemoglobin
      - 98% of  $O_2$  is carried by Hb
      - Capture oxygen in the alveoli, distributing it through the microcirculation, and ultimately discharging it in the pericellular environment

# Oxygen Delivery

- ▣  $DO_2 = Q \times CaO_2$ 
  - $Q = \text{Cardiac output} = \text{HR} \times \text{SV}$  (preload, afterload, contractility)
  - $CaO_2 = (1.34 \text{ Hb} \times SaO_2) + (PaO_2 \times 0.003)$



# Oxygen Consumption

- ▣ Oxygen consumption
  - $VO_2 = Q (CaO_2 - CvO_2)$ 
    - ▣ The amount of oxygen taken up by the cells ( $VO_2$ ) is a function of measuring cardiac output and the difference in arterial and venous oxygen consumption

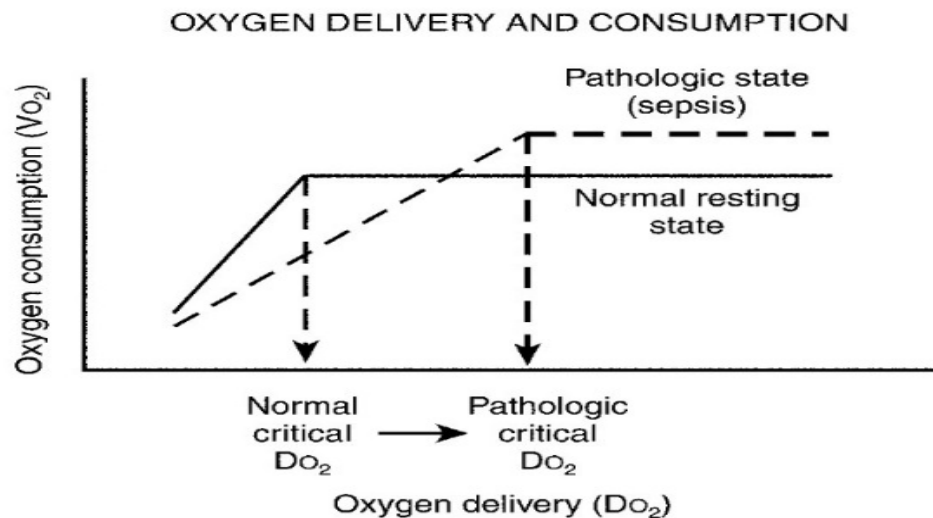


- ▣ Oxygen extraction ratio

- $O_2ER = (VO_2/DO_2)$

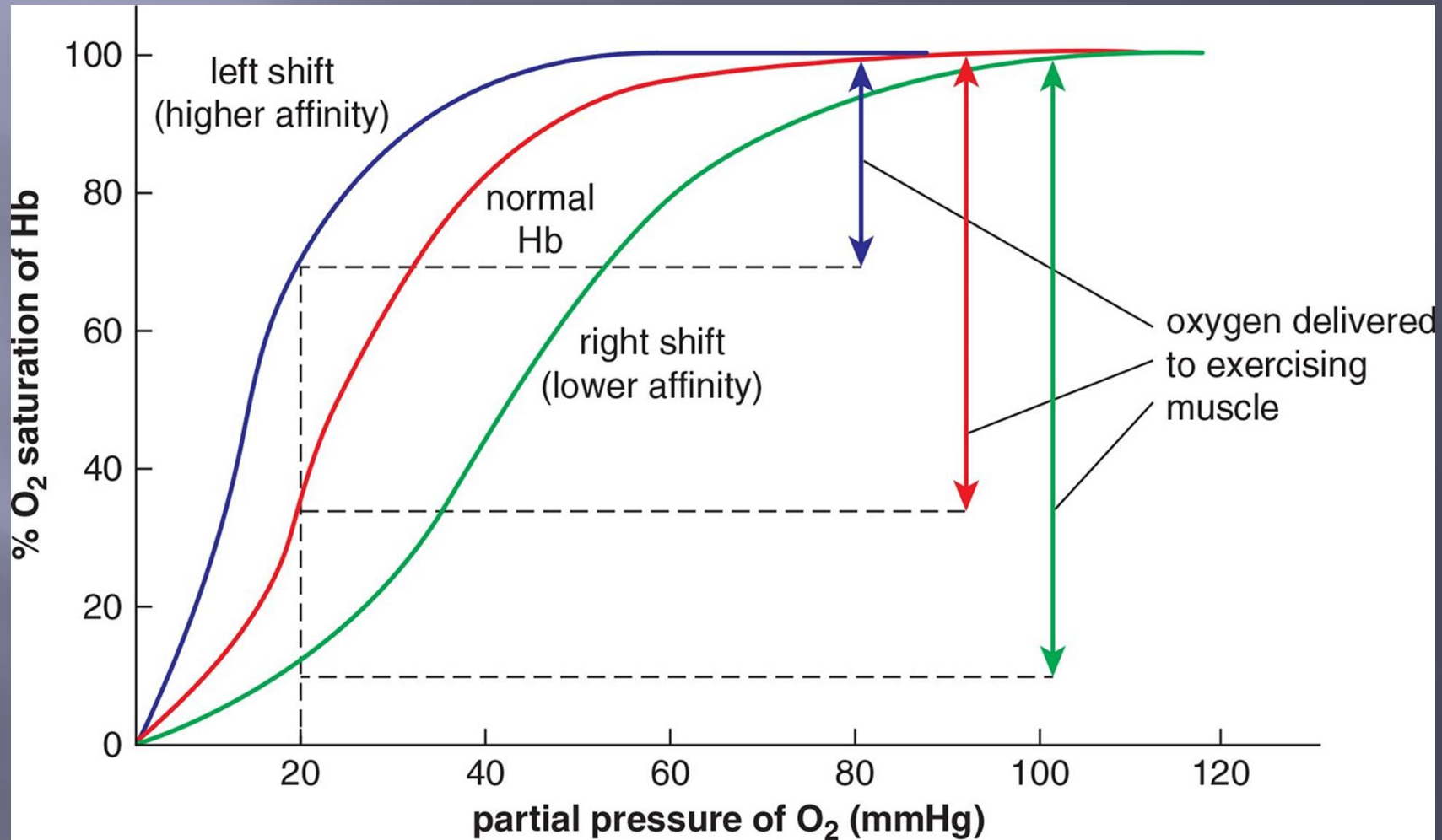
- ▣ Fractional uptake of oxygen by the tissues from the capillary bed, and thus, reflects the tissue's avidity for oxygen
    - ▣ 25% oxygen delivered is usually extracted

# Oxygen Delivery and Consumption



- $DO_2$  exceeds  $VO_2$ : oxygen consumption is independent of delivery
- Gradual decrease in delivery is associated with increase in  $O_2ER$  and aerobic metabolism maintained
- Critical  $DO_2$  when oxygen consumption becomes supply dependent and aerobic metabolism fails

# Oxyhemoglobin Dissociation Curve



# Anemia

## Clinical Setting

- ▣ Multifactorial
  - Failed erythropoiesis
  - Nutritional, metabolic, and hormonal derangements
  - Bone marrow impaired function
  - Pathologic (GI or other hemorrhage)
  - Iatrogenic (phlebotomy or interventional procedures)

# Restrictive Vs Liberal Transfusion Strategies

- ▣ Transfusion Triggers
  - 10/30 Rule
- ▣ 1988 National Institute Consensus Conference for Perioperative Blood Transfusion
  - No single criterion
  - Multiple factor
  - Optimize oxygen delivery





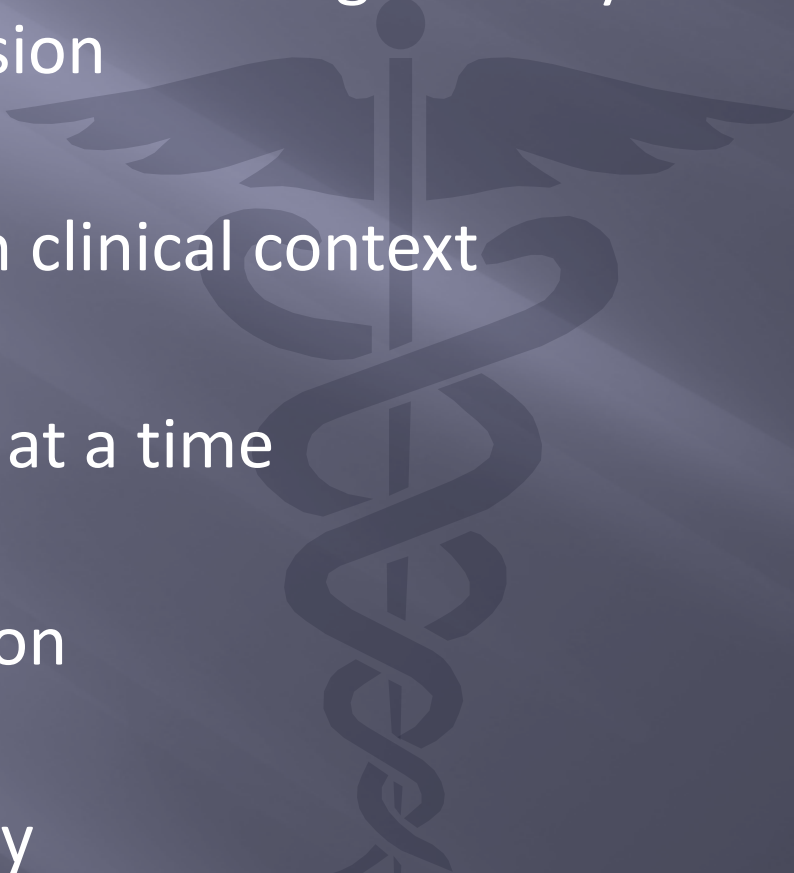
# Transfusion Complications

- ▣ Blood-borne infections
- ▣ Acute Immune Hemolytic Reactions
- ▣ Transfusion related acute lung injury (TRALI)
- ▣ Transfusion-associated circulatory overload (TACO)

# Transfusion

- ▣ “What would someone have to pay you to get a unit of blood that you didn’t need”

# Transfusion Strategies

- ▣ Transfusion based on maximizing delivery of oxygen without unnecessary transfusion
  - ▣ Transfusion based on clinical context
  - ▣ Transfusion one unit at a time
  - ▣ Triggers for transfusion
  - ▣ Minimize phlebotomy
- 

# Restrictive Vs Liberal Transfusion

- ▣ Restrictive (transfusion at lower Hgb level 7g/dl ; aiming for lower target hemoglobin)
- ▣ Liberal (transfusing at higher Hgb level 8-10 g/dl ; aiming for higher hemoglobin level)

# The New England Journal of Medicine

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VOLUME 340

FEBRUARY 11, 1999

NUMBER 6



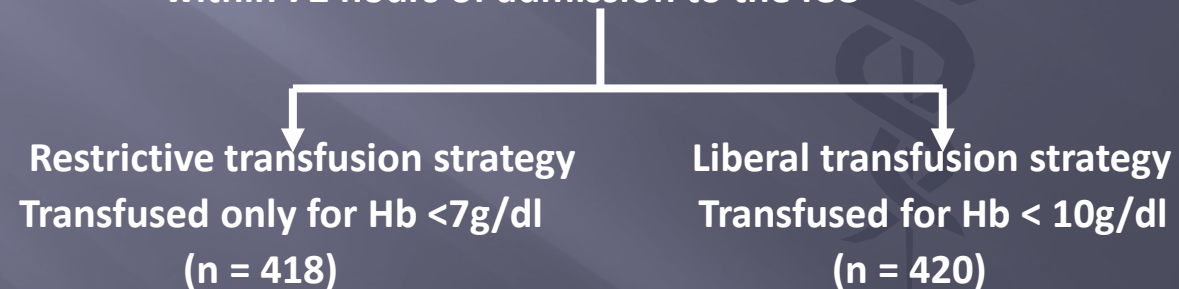
## A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

PAUL C. HÉBERT, M.D., GEORGE WELLS, PH.D., MORRIS A. BLAJCHMAN, M.D., JOHN MARSHALL, M.D.,  
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ELIZABETH YETISIR, M.Sc., AND THE TRANSFUSION REQUIREMENTS IN CRITICAL CARE INVESTIGATORS  
FOR THE CANADIAN CRITICAL CARE TRIALS GROUP\*

TRICC Trial

**Goal of the study:** To determine whether a restrictive strategy of PRBC transfusion and a liberal strategy of PRBC transfusion produced equivalent results in critically ill patients.

**Method:** 838 critically ill patients with Hb concentrations of < 9g/dl within 72 hours of admission to the ICU



## Results:

	Restrictive transfusion strategy	Liberal transfusion strategy	P Value
30 day mortality	18.7%	23.3%	0.11
Mortality during hospitalization	22.2%	28.1%	0.05
MSOF (> 3 organs)	5.3%	4.3%	0.36
Cardiac events (1° pulm edema and MI)	13.2%	21.0%	< 0.01
ARDS	7.7%	11.4%	0.06

There were no differences in 30 day mortality between treatment groups in the subgroup of patients with a primary or secondary diagnosis of cardiac disease.



## Success of Treatment:

The average daily hemoglobin concentrations were 8.5 +/- 0.7g/dl in the restrictive transfusion group and 10.7 +/- 0.7g/dl in the liberal-strategy group ( $p < 0.01$ ).

An average of 2.6 +/- 4.1 units of PRBCs per patient was administered to the restrictive-strategy group, compared with an average of 5.6 +/- 5.3 units per patient in the liberal-strategy group ( $p < 0.01$ ).

This equals a relative decrease of 54% in the number of transfusions when the lower threshold was used.

## Success of Treatment:

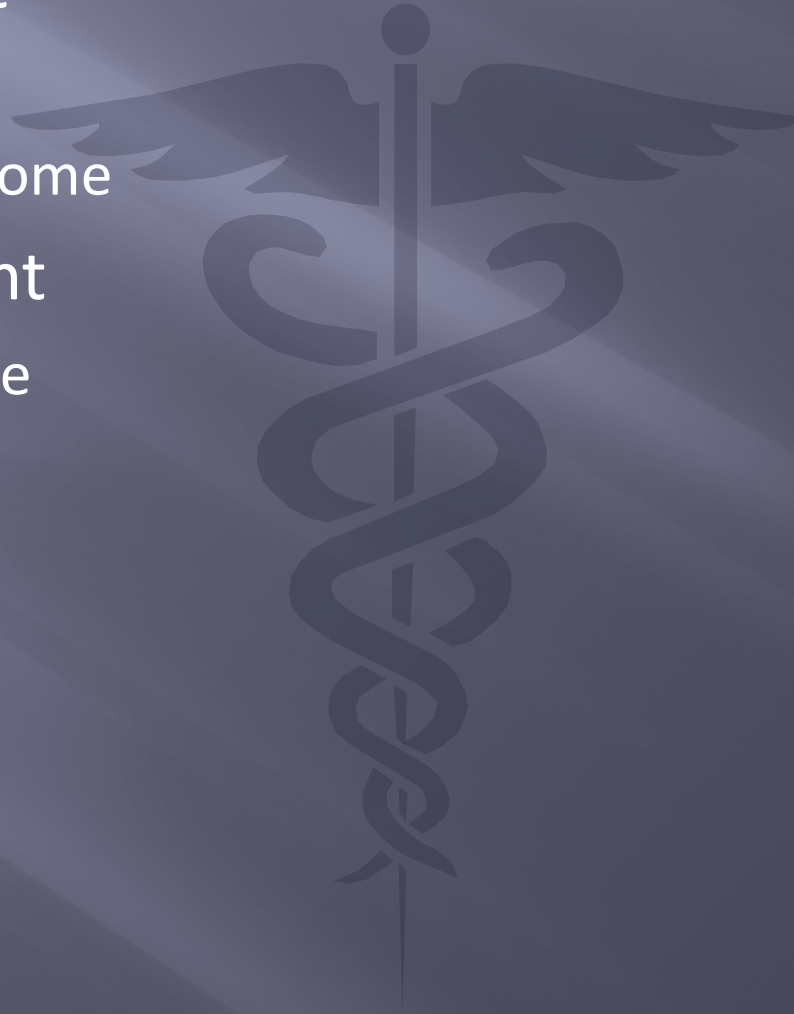
In addition, 33% of patients in the restrictive-strategy group did not receive any PRBCs after randomization, whereas all patients in the liberal-strategy group received at least 1 transfusion of PRBCs ( $p < 0.01$ ).

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

*N Eng J Med 340(6): 409, 1999*

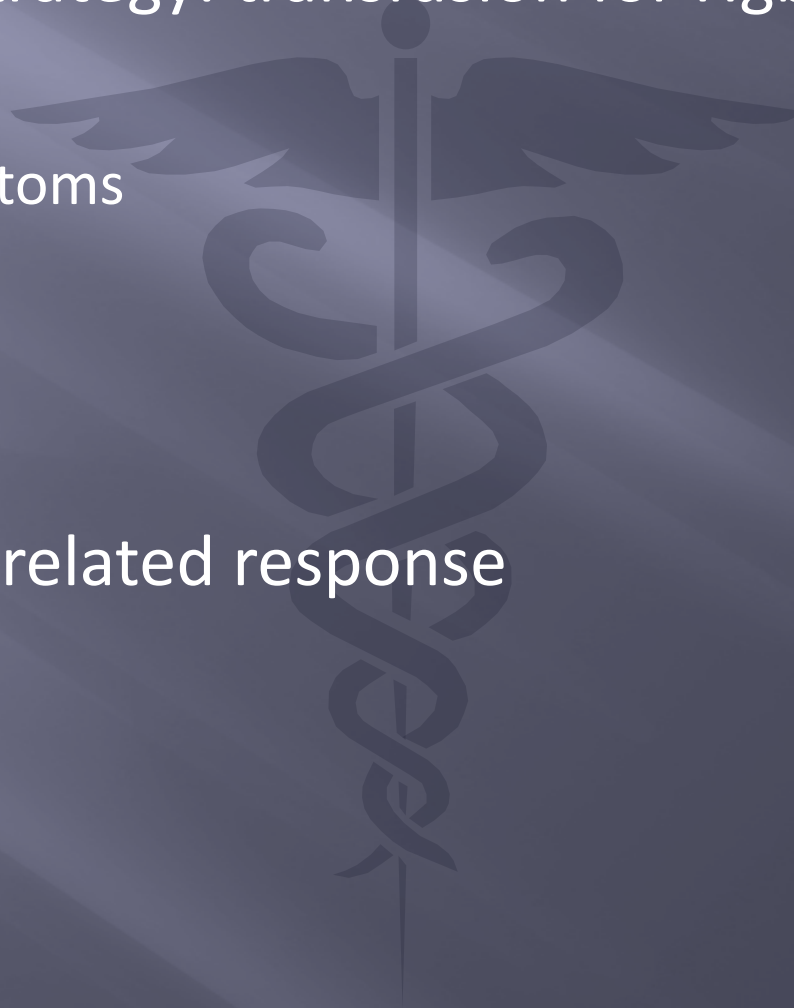
# Restrictive Vs Liberal Transfusion Strategies

- ▣ Symptomatic patient
  - Acute bleeding
  - Acute coronary syndrome
- ▣ Asymptomatic patient
  - Cardiovascular disease
  - Septic Shock
  - GI Bleed
  - Surgical patient
    - ▣ Cardiac Surgery



# Symptomatic Patient

- ▣ Liberal transfusion strategy: transfusion for Hgb <10g/dl
- ▣ Symptoms
  - Anemia related symptoms
  - Myocardial ischemia
  - Hypotension
  - Tachycardia
- ▣ Monitor transfusion related response



# Acute Bleeding

- ▣ Acute Bleeding
  - Hemodynamic parameters
  - Degree of bleeding and ability to stop
  - Use of transfusion in acutely hemorrhaging patients cannot be based on thresholds

# Transfusion Strategy

## Acute Bleeding

- ▣ Damage Control Resuscitation
  - Permissive Hypotension
  - Hemostatic Resuscitation (Massive Transfusion Protocol)
  - Hemorrhage Control (Damage Control Surgery)
  - 1:1:1 plasma:platelet:RBC



# PROMMTT Trial

## **The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study: Comparative Effectiveness of a Time-varying Treatment with Competing Risks**

**John B. Holcomb, MD<sup>1</sup>, Deborah J. del Junco, PhD<sup>1,2</sup>, Erin E. Fox, PhD<sup>2</sup>, Charles E. Wade, PhD<sup>1</sup>, Mitchell J. Cohen, MD<sup>3</sup>, Martin A. Schreiber, MD<sup>4</sup>, Louis H. Alarcon, MD<sup>5</sup>, Yu Bai, MD, PhD<sup>6</sup>, Karen J. Brasel, MD, MPH<sup>7</sup>, Eileen M. Bulger, MD<sup>8</sup>, Bryan A. Cotton, MD, MPH<sup>1</sup>, Nena Matijevic, PhD<sup>1</sup>, Peter Muskat, MD<sup>9</sup>, John G. Myers, MD<sup>10</sup>, Herb A. Phelan, MD, MSCS<sup>11</sup>, Christopher E. White, MD<sup>12</sup>, Jiajie Zhang, PhD<sup>13</sup>, and Mohammad H. Rahbar, PhD<sup>2,14</sup> for the PROMMTT Study Group**

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# PROMITT Trial

- ▣ Design—Prospective cohort study documenting the timing of transfusions during active resuscitation and patient outcomes. Ten US Level 1 trauma centers.
- ▣ Conclusions—Higher plasma and platelet ratios early in resuscitation were associated with decreased mortality in patients transfused at least three units of blood products during the first 24 hours after admission. Among survivors at 24 hours, the subsequent risk of death by day 30 was not associated with plasma or platelet ratios.

# PROPPR Trial

## **Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) Trial: Design, rationale and implementation**

**Sarah Baraniuk<sup>1</sup>, Barbara C. Tilley<sup>1</sup>, Deborah J. del Junco<sup>2</sup>, Erin E. Fox<sup>2</sup>, Gerald van Belle<sup>3</sup>, Charles E. Wade<sup>2</sup>, Jeanette M. Podbielski<sup>2</sup>, Angela M. Beeler<sup>2</sup>, John R. Hess<sup>3</sup>, Eileen M. Bulger<sup>4</sup>, Martin A. Schreiber<sup>5</sup>, Kenji Inaba<sup>6</sup>, Timothy C. Fabian<sup>7</sup>, Jeffrey D. Kerby<sup>8</sup>, Mitchell J. Cohen<sup>9</sup>, Christopher N. Miller<sup>10</sup>, Sandro Rizoli<sup>11</sup>, Thomas M. Scalea<sup>12</sup>, Terence O’Keeffe<sup>13</sup>, Karen J. Brasel<sup>14</sup>, Bryan A. Cotton<sup>2</sup>, Peter Muskat<sup>15</sup>, John B. Holcomb<sup>2</sup>, and the PROPPR Study Group**

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# PROPPR Trial

- ▣ DESIGN, SETTING, AND PARTICIPANTS Pragmatic, phase 3, multisite, randomized clinical trial of 680 severely injured patients who arrived at 1 of 12 level I trauma centers in North America directly from the scene and were predicted to require massive transfusion between August 2012 and December 2013.
- ▣ INTERVENTIONS: Blood product ratios of 1:1:1 (338 patients) vs 1:1:2 (342 patients) during active resuscitation in addition to all local standard-of-care interventions (uncontrolled).

# PROPPR Trial

- ▣ Among patients with severe trauma and major bleeding, early administration of plasma, platelets, and red blood cells in a 1:1:1 ratio vs 1:1:2 ratio did not result in significant differences in mortality at 24 hours or 30 days.
- ▣ 1:1:1 transfusion decreases death from exsanguination at 24 hours, achieves more rapid hemostasis, and has no additional complications



# Acute Coronary Syndrome

## Liberal Versus Restrictive Transfusion Thresholds For Patients With Symptomatic Coronary Artery Disease

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### Abstract

**Background**—Prior trials suggest it is safe to defer transfusion at hemoglobin levels above 7–8 g/dL in most patients. Patients with acute coronary syndrome may benefit from higher hemoglobin levels.

**Methods**—We performed a pilot trial in 110 patients with acute coronary syndrome or stable angina undergoing cardiac catheterization and a hemoglobin < 10 g/dL. Patients in the liberal transfusion strategy received one or more units of blood to raise the hemoglobin level  $\geq$  10 g/dL. Patients in the restrictive transfusion strategy were permitted to receive blood for symptoms from anemia or for a hemoglobin < 8 g/dL. The predefined primary outcome was the composite of death, myocardial infarction, or unscheduled revascularization 30 days post randomization.



# Acute Coronary Syndrome

- ▣ **Methods**—Pilot trial in 110 patients with acute coronary syndrome or stable angina undergoing cardiac catheterization and a hemoglobin < 10 g/dL.
  - Liberal one or more units of blood to raise the hemoglobin level  $\geq 10$  g/dL.
  - Patients in the restrictive transfusion strategy were permitted to receive blood for symptoms from anemia or for a hemoglobin < 8 g/dL.
- ▣ The liberal transfusion strategy was associated with a trend for fewer major cardiac events and deaths than a more restrictive strategy.

# Acute Coronary Syndrome

- ▣ Liberal transfusion strategy with trigger hemoglobin  $<8$  g/dl and to consider transfusion between hemoglobin 8 and 10 g/dl
- ▣ If ongoing ischemia maintain the hemoglobin  $> 10$ g/dl
- ▣ In stable, asymptomatic patients post intervention (medical or interventional), maintain higher hemoglobin transfusion trigger  $<8$ g/dl, use clinical judgement based on symptoms and underlying condition

# Asymptomatic Cardiovascular Disease

## Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

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### Abstract

**BACKGROUND**—The hemoglobin threshold at which postoperative red-cell transfusion is warranted is controversial. We conducted a randomized trial to determine whether a higher threshold for blood transfusion would improve recovery in patients who had undergone surgery for hip fracture.

**METHODS**—We enrolled 2016 patients who were 50 years of age or older, who had either a history of or risk factors for cardiovascular disease, and whose hemoglobin level was below 10 g per deciliter after hip-fracture surgery. We randomly assigned patients to a liberal transfusion strategy (a hemoglobin threshold of 10 g per deciliter) or a restrictive transfusion strategy (symptoms of anemia or at physician discretion for a hemoglobin level of <8 g per deciliter). The primary outcome was death or an inability to walk across a room without human assistance on 60-day follow-up.

**RESULTS**—A median of 2 units of red cells were transfused in the liberal-strategy group and none in the restrictive-strategy group. The rates of the primary outcome were 35.2% in the liberal-strategy group and 34.7% in the restrictive-strategy group (odds ratio in the liberal-strategy group, 1.01; 95% confidence interval [CI], 0.84 to 1.22), for an absolute risk difference of 0.5 percentage points (95% CI, -3.7 to 4.7). The rates of in-hospital acute coronary syndrome or death were 4.3% and 5.2%, respectively (absolute risk difference, -0.9%; 99% CI, -3.3 to 1.6), and rates of death on 60-day follow-up were 7.6% and 6.6%, respectively (absolute risk difference, 1.0%; 99% CI, -1.9 to 4.0). The rates of other complications were similar in the two groups.

**CONCLUSIONS**—A liberal transfusion strategy, as compared with a restrictive strategy, did not reduce rates of death or inability to walk independently on 60-day follow-up or reduce in-hospital morbidity in elderly patients at high cardiovascular risk. (Funded by the National Heart, Lung, and Blood Institute; FOCUS ClinicalTrials.gov number, NCT00071032.)

# Asymptomatic Cardiovascular Disease

- ▣ Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS), compared with threshold 10g/dl, a transfusion strategy of 8g/dl after hip fracture surgery
- ▣ A liberal transfusion strategy (10g/dl), as compared to restrictive (8g/dl), did not reduce rates of death or inability to walk independently on 60-day follow-up or reduce in-hospital morbidity in elderly patients at high cardiovascular risk
- ▣ Transfusion trigger 8g/dl, but consideration of transfusion in patient between 8-10g/dl based on symptoms and underlying condition



# Asymptomatic Septic Shock

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

OCTOBER 9, 2014

VOL. 371 NO. 15

### Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock

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#### ABSTRACT

#### BACKGROUND

Blood transfusions are frequently given to patients with septic shock. However, the benefits and harms of different hemoglobin thresholds for transfusion have not been established.

#### METHODS

In this multicenter, parallel-group trial, we randomly assigned patients in the intensive care unit (ICU) who had septic shock and a hemoglobin concentration of 9 g per deciliter or less to receive 1 unit of leukoreduced red cells when the hemoglobin level was 7 g per deciliter or less (lower threshold) or when the level was 9 g per deciliter or less (higher threshold) during the ICU stay. The primary outcome measure was death by 90 days after randomization.

#### RESULTS

We analyzed data from 998 of 1005 patients (99.3%) who underwent randomization. The two intervention groups had similar baseline characteristics. In the ICU, the lower-threshold group received a median of 1 unit of blood (interquartile range, 0 to 3) and the higher-threshold group received a median of 4 units (interquartile range, 2 to 7). At 90 days after randomization, 216 of 502 patients (43.0%) assigned to the lower-threshold group, as compared with 223 of 496 (45.0%) assigned to the higher-threshold group, had died (relative risk, 0.94; 95% confidence interval, 0.78 to 1.09;  $P=0.44$ ). The results were similar in analyses adjusted for risk factors at baseline and in analyses of the per-protocol populations. The numbers of patients who had ischemic events, who had severe adverse reactions, and who required life support were similar in the two intervention groups.

#### CONCLUSIONS

Among patients with septic shock, mortality at 90 days and rates of ischemic events and use of life support were similar among those assigned to blood transfusion at a higher hemoglobin threshold and those assigned to blood transfusion at a lower threshold; the latter group received fewer transfusions. (Funded by the Danish Strategic Research Council and others; TRISS ClinicalTrials.gov number, NCT01485315.)

From the Department of Intensive Care (L.B.H., N.H., L.H.A., U.G.P., N.R., J. Wiis, J.O.W., L.R., K.J.T., P.B.H., R.G.M., M.H.M., M.S., A.P.), Copenhagen Trial Unit, Center for Clinical Intervention Research (J. Wetterslev, P.W.), and Section for Transfusion Medicine (P.I.J.), Rigshospitalet and University of Copenhagen, Copenhagen, Denmark; Randers Hospital, Randers (M.L.V., H.B., M.A.T.), Herning Hospital, Herning (R.W., D.L., R.M.), Hvidovre Hospital, Hvidovre (L.N., C.A.), Aarhus University Hospital, Aarhus (H.L.N., D.I.), Aalborg University Hospital, Aalborg (B.S.R.), Holbæk Hospital, Holbæk (J.R.M.L.), Kolding Hospital, Kolding (J.S.N.), and Hjørring Hospital, Hjørring (M.K.) — all in Denmark; Karolinska University Hospital, Huddinge, Stockholm (J. Wernerman, I.T., K.K., S.O.-W.), Karolinska University Hospital, Solna (A.O.), and Södersjukhuset, Stockholm (M.B.C.) — all in Sweden; Haukeland University Hospital and University of Bergen, Bergen, Norway (A.B.G., B.S.); Tampere University Hospital, Tampere (S.K.), and Helsinki University Hospital and University of Helsinki, Helsinki (V.P.) — all in Finland; and Liverpool Hospital, Sydney (A.A.). Address reprint requests to Dr. Perner at the Department of Intensive Care, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark, or at anders.perner@regionh.dk.

\*Members of the Transfusion Requirements in Septic Shock (TRISS) Trial Group are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on October 1, 2014, at NEJM.org.

N Engl J Med 2014;371:1381-91.  
DOI: 10.1056/NEJMoa1406617  
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# Asymptomatic Septic Shock

- ▣ Transfusion Requirements in Septic Shock (TRISS)
- ▣ 998 patients with septic shock to restrictive or liberal transfusion strategy (transfusion at hgb  $\leq 7$ g/dl or  $\leq 9$ g/dl)
- ▣ 90 day mortality, rates of ischemic events, and use of life support were similar with less transfusion in restrictive group



# Asymptomatic GI Bleed

## Restrictive versus liberal blood transfusion for acute upper gastrointestinal bleeding (TRIGGER): a pragmatic, open-label, cluster randomised feasibility trial

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### Summary

**Background** Transfusion thresholds for acute upper gastrointestinal bleeding are controversial. So far, only three small, underpowered studies and one single-centre trial have been done. Findings from the single-centre trial showed reduced mortality with restrictive red blood cell (RBC) transfusion. We aimed to assess whether a multicentre, cluster randomised trial is a feasible method to substantiate or refute this finding.

**Methods** In this pragmatic, open-label, cluster randomised feasibility trial, done in six university hospitals in the UK, we enrolled all patients aged 18 years or older with new presentations of acute upper gastrointestinal bleeding, irrespective of comorbidity, except for exsanguinating haemorrhage. We randomly assigned hospitals (1:1) with a computer-generated randomisation sequence (random permuted block size of 6, without stratification or matching) to either a restrictive (transfusion when haemoglobin concentration fell below 80 g/L) or liberal (transfusion when haemoglobin concentration fell below 100 g/L) RBC transfusion policy. Neither patients nor investigators were masked to treatment allocation. Feasibility outcomes were recruitment rate, protocol adherence, haemoglobin concentration, RBC exposure, selection bias, and information to guide design and economic evaluation of the phase 3 trial. Main exploratory clinical outcomes were further bleeding and mortality at day 28. We did analyses on all enrolled patients for whom an outcome was available. This trial is registered, ISRCTN85757829 and NCT02105532.

**Findings** Between Sept 3, 2012, and March 1, 2013, we enrolled 936 patients across six hospitals (403 patients in three hospitals with a restrictive policy and 533 patients in three hospitals with a liberal policy). Recruitment rate was significantly higher for the liberal than for the restrictive policy (62% vs 55%;  $p=0.04$ ). Despite some baseline imbalances, Rockall and Blatchford risk scores were identical between policies. Protocol adherence was 96% (SD 10) in the restrictive policy vs 83% (25) in the liberal policy (difference 14%; 95% CI 7–21;  $p=0.005$ ). Mean last recorded haemoglobin concentration was 116 (SD 24) g/L for patients on the restrictive policy and 118 (20) g/L for those on the liberal policy (difference  $-2.0$  [95% CI  $-12.0$  to  $7.0$ ];  $p=0.50$ ). Fewer patients received RBCs on the restrictive policy than on the liberal policy (restrictive policy 133 [33%] vs liberal policy 247 [46%]; difference  $-12\%$  [95% CI  $-35$  to  $11$ ];  $p=0.23$ ), with fewer RBC units transfused (mean  $1.2$  [SD  $2.1$ ] vs  $1.9$  [2.8]; difference  $-0.7$  [ $-1.6$  to  $0.3$ ];  $p=0.12$ ), although these differences were not significant. We noted no significant difference in clinical outcomes.

**Interpretation** A cluster randomised design led to rapid recruitment, high protocol adherence, separation in degree of anaemia between groups, and non-significant reduction in RBC transfusion in the restrictive policy. A large cluster randomised trial to assess the effectiveness of transfusion strategies for acute upper gastrointestinal bleeding is both feasible and essential before clinical practice guidelines change to recommend restrictive transfusion for all patients with acute upper gastrointestinal bleeding.

# Asymptomatic GI Bleed

- ▣ Multicenter trial that randomly assigned 936 patients with acute upper GI bleed to restrictive or liberal threshold (8g/dl versus 10g/dl) found no significant difference in clinical outcomes; fewer transfusions were given in restrictive group
- ▣ Lower transfusion trigger in hemodynamically stable patient; without unstable coronary disease; and access to rapid endoscopic/surgical intervention, restrictive strategy maybe safe

# Asymptomatic Cardiac Surgery

## Clinical trials evaluating red blood cell transfusion thresholds: An updated systematic review and with additional focus on patients with cardiovascular disease



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### ARTICLE INFO

#### Article history:

Received 8 February 2018

Accepted 3 April 2018

### ABSTRACT

**Background:** Several new trials evaluating transfusion strategies in patients with cardiovascular disease have recently been published, increasing the number of enrolled patients by over 30%. The objective was to evaluate transfusion thresholds in patients with cardiovascular disease.

**Methods:** We conducted an updated systematic review of randomized trials that compared patients assigned to maintain a lower (restrictive transfusion strategy) or higher (liberal transfusion strategy) hemoglobin concentration. We focused on new trial data in patients with cardiovascular disease. The primary outcome was 30-day mortality. Specific subgroups were patients undergoing cardiac surgery and with acute myocardial infarction.

**Results:** A total of 37 trials that enrolled 19,049 patients were appraised. In cardiac surgery, mortality at 30 days was comparable between groups (risk ratio 0.99; 95% confidence interval 0.74-1.33). In 2 small trials (n = 154) in patients with myocardial infarction, the point estimate for the mortality risk ratio was 3.88 (95% CI, 0.83-18.13) favoring the liberal strategy. Overall, from 26 trials enrolling 15,681 patients, 30-day mortality was not different between restrictive and liberal transfusion strategies (risk ratio 1.0, 95% CI, 0.86-1.16). Overall and in the cardiovascular disease subgroup, there were no significant differences observed across a range of secondary outcomes.

**Conclusions:** New trials in patients undergoing cardiac surgery establish that a restrictive transfusion strategy of 7 to 8 g/dL is safe and decreased red cell use by 24%. Further research is needed to define the optimal transfusion threshold in patients with acute myocardial infarction.

# Asymptomatic Cardiac Surgery

- ▣ Transfusion thresholds in cardiac surgery have been evaluated in multiple randomized trials.
- ▣ 2018 meta-analysis that a restrictive transfusion strategy with hemoglobin threshold of 7.5 to 8 g/dl in cardiac surgery patients is safe, and decreased red cell use by 24%.



# AABB Guidelines

JAMA | Special Communication

## Clinical Practice Guidelines From the AABB Red Blood Cell Transfusion Thresholds and Storage

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**IMPORTANCE** More than 100 million units of blood are collected worldwide each year, yet the indication for red blood cell (RBC) transfusion and the optimal length of RBC storage prior to transfusion are uncertain.

**OBJECTIVE** To provide recommendations for the target hemoglobin level for RBC transfusion among hospitalized adult patients who are hemodynamically stable and the length of time RBCs should be stored prior to transfusion.

**EVIDENCE REVIEW** Reference librarians conducted a literature search for randomized clinical trials (RCTs) evaluating hemoglobin thresholds for RBC transfusion (1950-May 2016) and RBC storage duration (1948-May 2016) without language restrictions. The results were summarized using the Grading of Recommendations Assessment, Development and

← Editorial page 1984

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- ▣ Transfusion triggers
  - Hemoglobin level
  - Clinical context
  - Patient preferences
  - Alternative therapies

# AABB

## Recommendations

- ▣ Hemoglobin <6 g/dl – Transfusion recommended except in exceptional circumstances





# AABB

## Recommendations

- ▣ Hemoglobin 6 to 7 g/dl – Transfusion generally indicated



# AABB

## Recommendations

- ▣ Hemoglobin 7 to 8 g/dl – transfusion may be appropriate in patients undergoing orthopedic surgery or cardiac surgery, and in those with stable cardiovascular disease, after evaluating the patient's clinical status

# AABB

## Recommendations

- ▣ Hemoglobin 8 to 10 g/dl – Transfusion generally not indicated, but should be considered for some populations (symptomatic anemia, ongoing bleeding, acute coronary syndrome with ischemia, and hem-oncology patient with severe thrombocytopenia who are at risk for bleeding)

# AABB

## Recommendations

- ▣ Hemoglobin >10 g/dl – Transfusion generally not indicated except in exceptional circumstances



# Summary

- ▣ Optimization of oxygen delivery during pathologic state curtails anaerobic metabolism
- ▣ Restrictive versus liberal blood transfusion is safe for most critically ill patients
- ▣ Transfusion decision is multi-factorial

# Question 1

- A. 16 y/o s/p skate boarding accident arrives per private vehicle. Patient transported through triage immediately to trauma activation bay. Patient is diaphoretic, confused, pallor, with the following vital signs: HR:165 BP: 65/40 RR:35 O2Sat's: 92% RA. How would you manage his transfusion requirements.
- a) Type and cross, stat labs, transfuse 2 units of cross matched blood
  - b) Bolus two liters of crystalloids, type and cross, send stat labs
  - c) Initiate massive transfusion protocol, emergency release prbc, liquid plasma, minimize crystalloids, allow for permissive hypotension until source control
  - d) Bolus liter crystalloid, bolus 500cc 5% albumin, type and cross, transfuse based on response to fluid bolus



# Answer

- ▣ Initiate massive transfusion protocol, emergency release prbc, liquid plasma, minimize crystalloids, allow for permissive hypotension until source control



## Question 2

- ▣ 56 y/o woman arrives with acute chest pain to emergency room. Patient is complaining of chest pain with ST elevations on EKG, elevated troponins. Patient has stat labs sent with admission hemoglobin of 8g/dl. Patient vitals: HR:110 BP: 176/100 RR: 32 O2 sats: 96% RA
  - a) No transfusion
  - b) Repeat labs post heart catheterization and transfusion for  $\leq 7\text{g/dl}$
  - c) Transfuse one unit prbc
  - d) Start inotropic gtt to optimize cardiac output

## Answer 2

- ▣ Transfuse one unit prbc



## Question 3

- ▣ 68 y/o s/p UGI bleed with known history of bleeding ulcer. Patient with failed endoscopy with active bleeding. Patient has hemoglobin 9 g/dl, and currently is awaiting interventional radiology.
  - a) Liberal transfusion strategy to  $>10$  g/dl in an actively bleeding patient
  - b) Serial hemoglobin measurements every 6 hours transfuse for Hgb  $<8$  g/dl
  - c) Await episode of hypotension and tachycardia, and transfuse one unit at that time
  - d) Restrictive transfusion strategy, await for Hgb  $<7$  g/dl

## Answer 3

- ▣ Liberal transfusion strategy to  $>10$  g/dl in an actively bleeding patient



## Question 4

- ▣ 87 y/o s/p fall from standing undergoes hip fracture surgery, she has known history of cardiovascular disease. Postoperative day 1 she has the following vital signs HR: 67 BP: 157/85 RR: 22 O2 Sat's:94% RA. Patients Hgb/Hct this morning is 8.5/25.5, what is your next step?
  - a) Transfuse one unit prbc
  - b) Serial H/H to monitor anemia over the next 24 hours
  - c) Hold transfuse, transfuse for hgb <8g/dl and/or any symptoms of anemia
  - d) Albumin and Lasix



## Question 4

- ▣ Hold transfuse, transfuse for hgb <8g/dl and/or any symptoms of anemia

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