SABM®
SOCIETY FOR THE ADVANCEMENT OF PATIENT BLOOD MANAGEMENT

IMPROVEMENT OF PATIENT OUTCOMES WITH HEMOGLOBIN MONITORING

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Clinical Professor of Anesthesiology Rutgers Medical School, New Jersey

TEAMHealth ANESTHESIA

ENGLEWOOD HEALTH

DISCLOSURE 1

SPEAKERS BUREAU: Merck

CONSULTANT/SPEAKER: Masimo Corporation, CSL Behring, Gauss Surgical, Vifor Pharma, Octapharma and Pharmaniaga

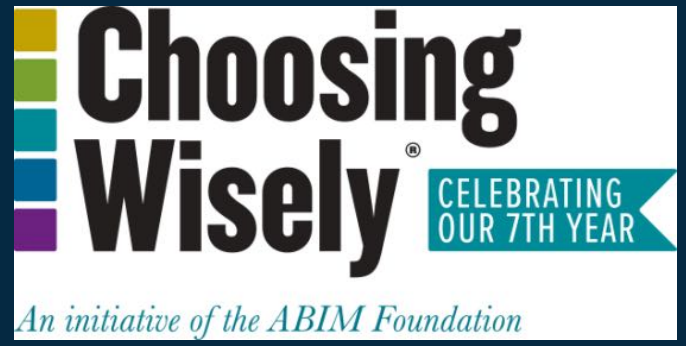
GRANT/RESEARCH: CSL Behring, Masimo, HbO2 Therapeutics, LLC

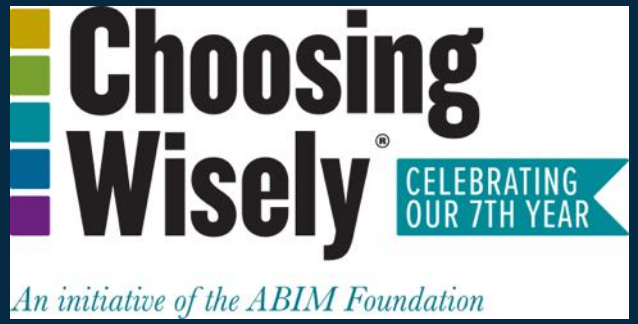
DISCLOSURE 2

CONSULTANT: USDOD, USDOJ AND USDHHS

OVERVIEW

- What is PBM and why in the ICU?
- Treating numbers vs. patients
- Prevalence of anemia in ICU
- Consequences of anemia, transfusions
- Anemia causes (Etiology in critically ill patients)
- “New” concept of iatrogenic anemia (SpHb)
- Applying PBM in the ICU





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The mission of *Choosing Wisely* is to promote conversations between clinicians and patients by helping patients choose care that is:

- Supported by evidence
- Not duplicative of other tests or procedures already received
- Free from harm
- Truly necessary

2012

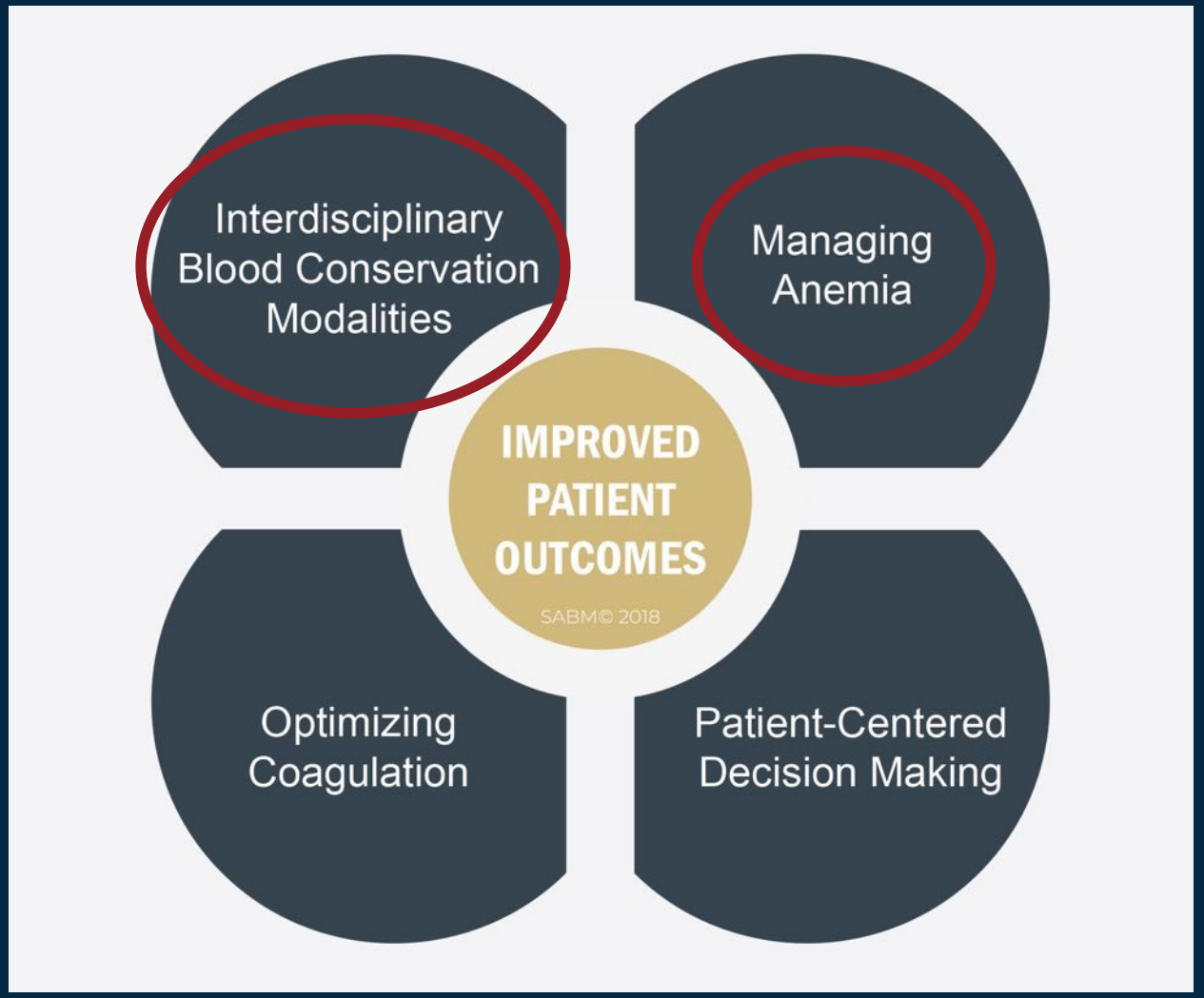
ABIM FOUNDATION

SABM DEFINITION OF PBM

"The timely application of evidence based medical and surgical concepts designed to manage anemia, optimize hemostasis, and minimize blood loss in order to improve **patient outcomes**."

Patient focused – Medical condition (disease) focused

PATIENT BLOOD MANAGEMENT

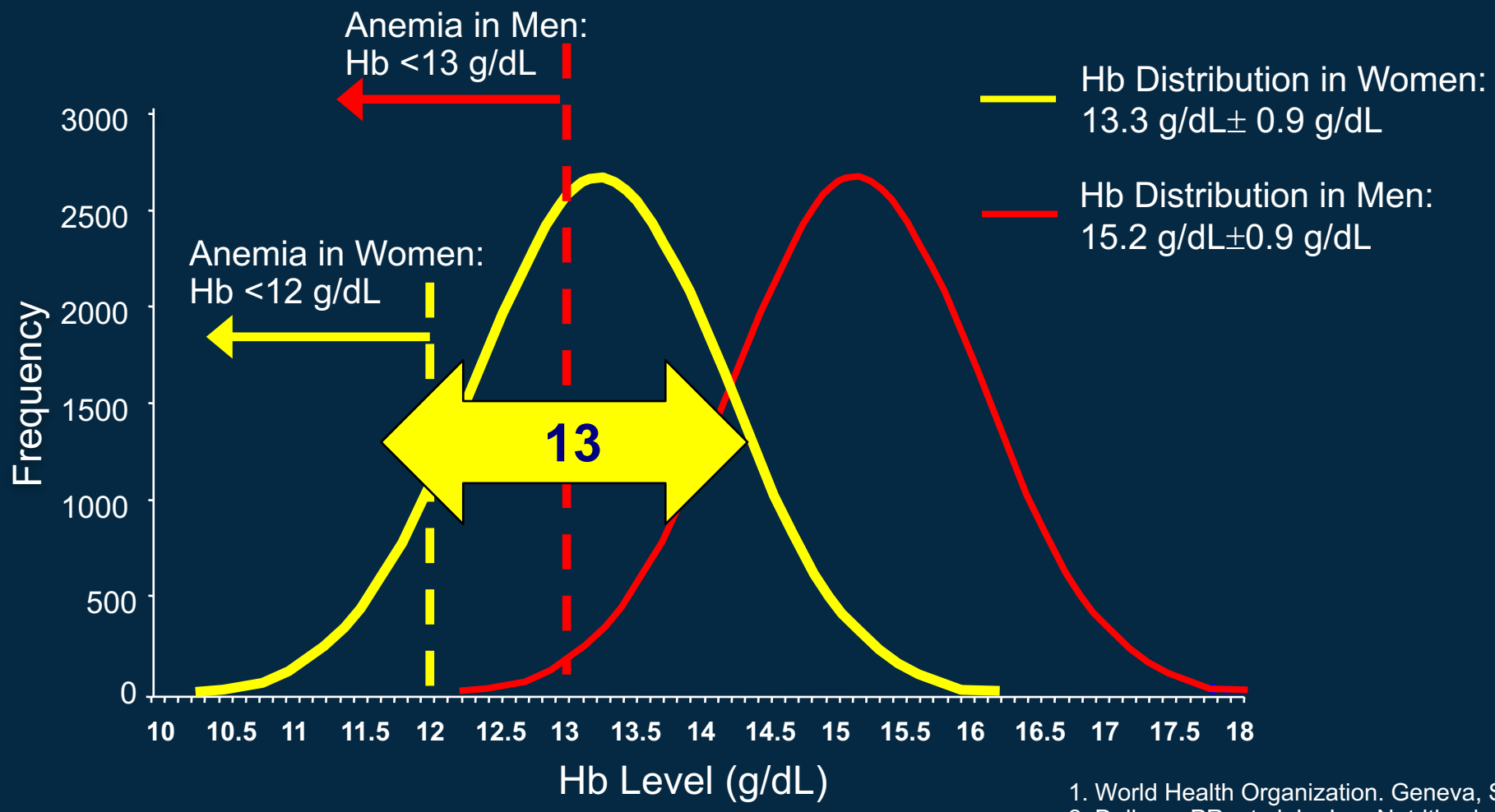


PREVALENCE OF ANEMIA IN THE CRITICALLY ILL

- Sakr et al reported anemia in the ICU - 18.7% had Hb <7 g/dL and 29.5% had 7-9 g/dL[1]
- Cardenas-Turanzas et al reported an incidence of 46.6% and prevalence of 68% of anemia in cancer patients admitted to ICU[2]
- Thomas et al reported that 98 of 100 consecutive patients admitted to ICU were anemic[3]
- Anemia was associated with increased risk of allogeneic blood transfusion[1]
- Higher Hb level was independently associated with lower risk of in-hospital death[1]

1. Sakr Y et al. Crit Care 2010
2. Cardenas-Turanzas M etal. J Crit Care 2010
3. 3. Thomas J et al. Heart Lung 2010

WHO DEFINITION OF ANEMIA VS Hb DISTRIBUTION IN GENERAL POPULATION



1. World Health Organization. Geneva, Switzerland; 2001.
2. Dallman PR, et al. In: Iron Nutrition in Health and Disease London, UK: John Libbey& Co; 1996:65-74.

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Haematocrit is invalid for estimating red cell volume: a prospective study in male volunteers

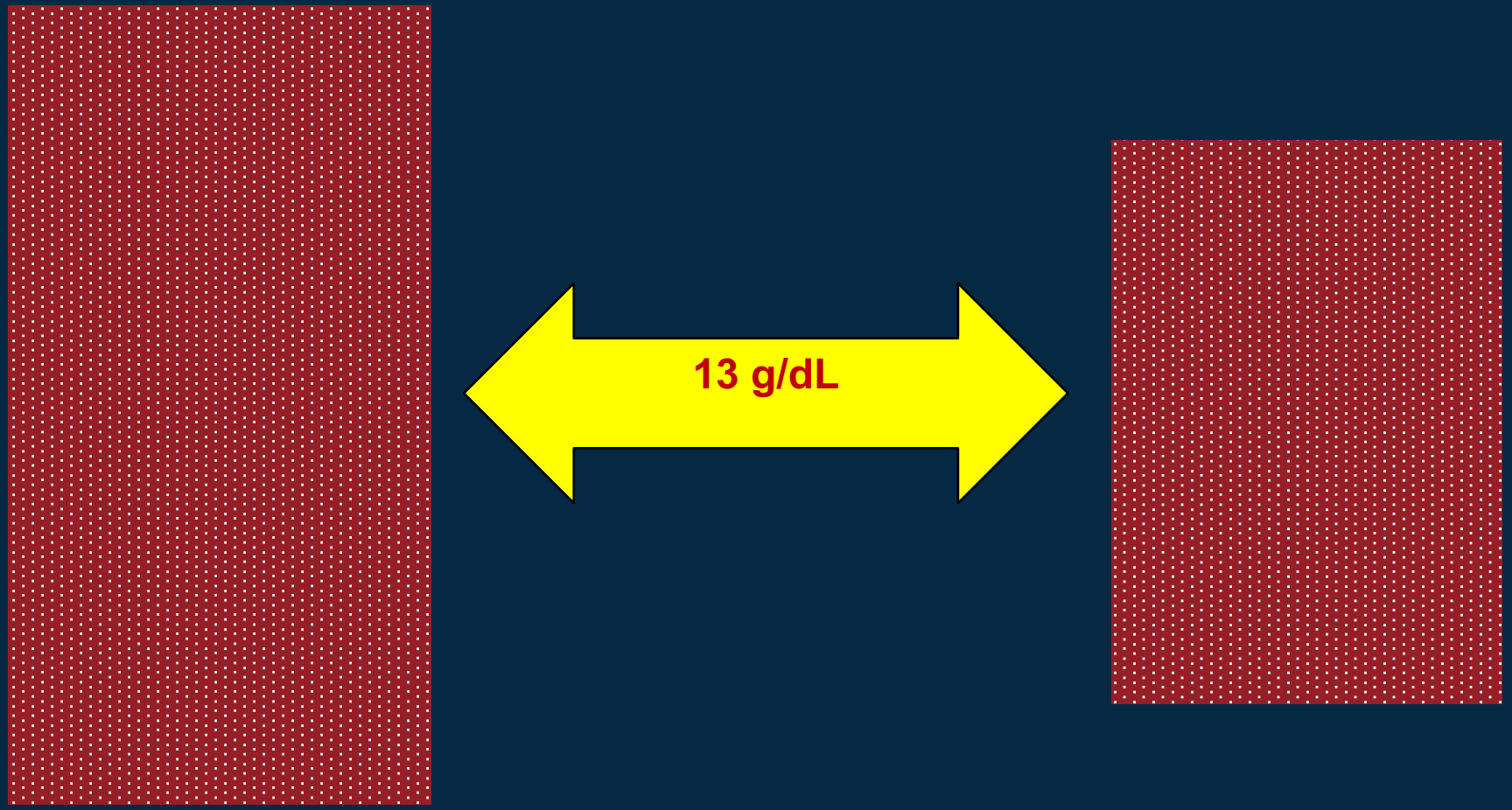
Matthias Jacob[1], Simon Annaheim[2], Urs Boutellier[2], Christian Hinske[1], Markus Rehm[1], Christian Breymann[3], Alexander Krafft[3]

- N = 46 healthy male endurance athletes
- Red cell volume (2,282±283 mL) did not correlate with either hct (0.42±0.02) or hb conc (14.2±0.8, P>0.05, resp.)
- RCV was predictable from body surface area (P<0.01)
- A similar accuracy was unobtainable using any potential predictor for plasma or blood volume, hct or hb concentration
- RCV showed high intra-individual stability when measured again after 4 weeks, whereas plasma volume oscillated in both directions by up to 22%

Hemoglobin is a concentration measure – meaningless alone

Blood Transfus. 2012

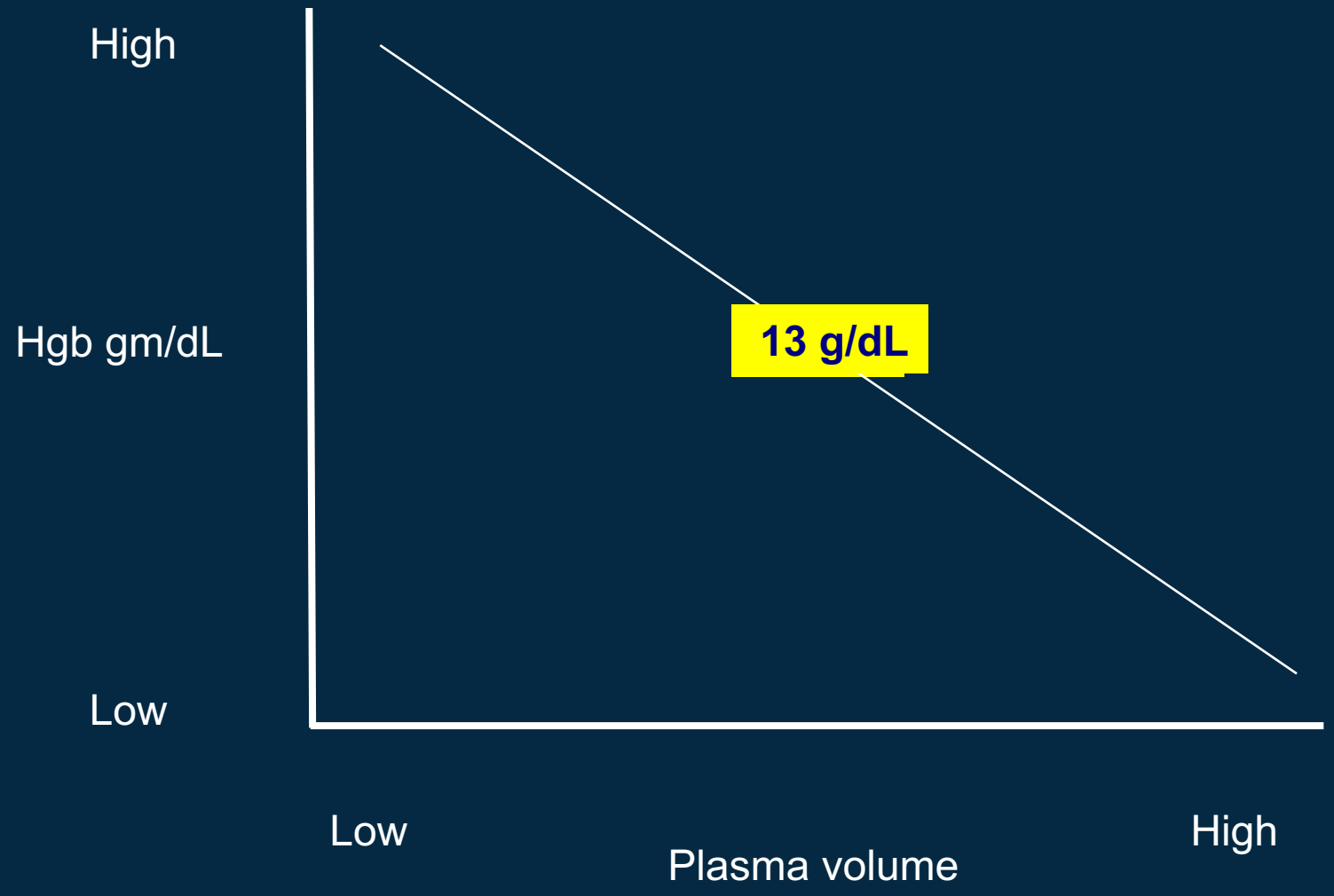
RED CELL MASS VS. HEMOGLOBIN CONCENTRATION



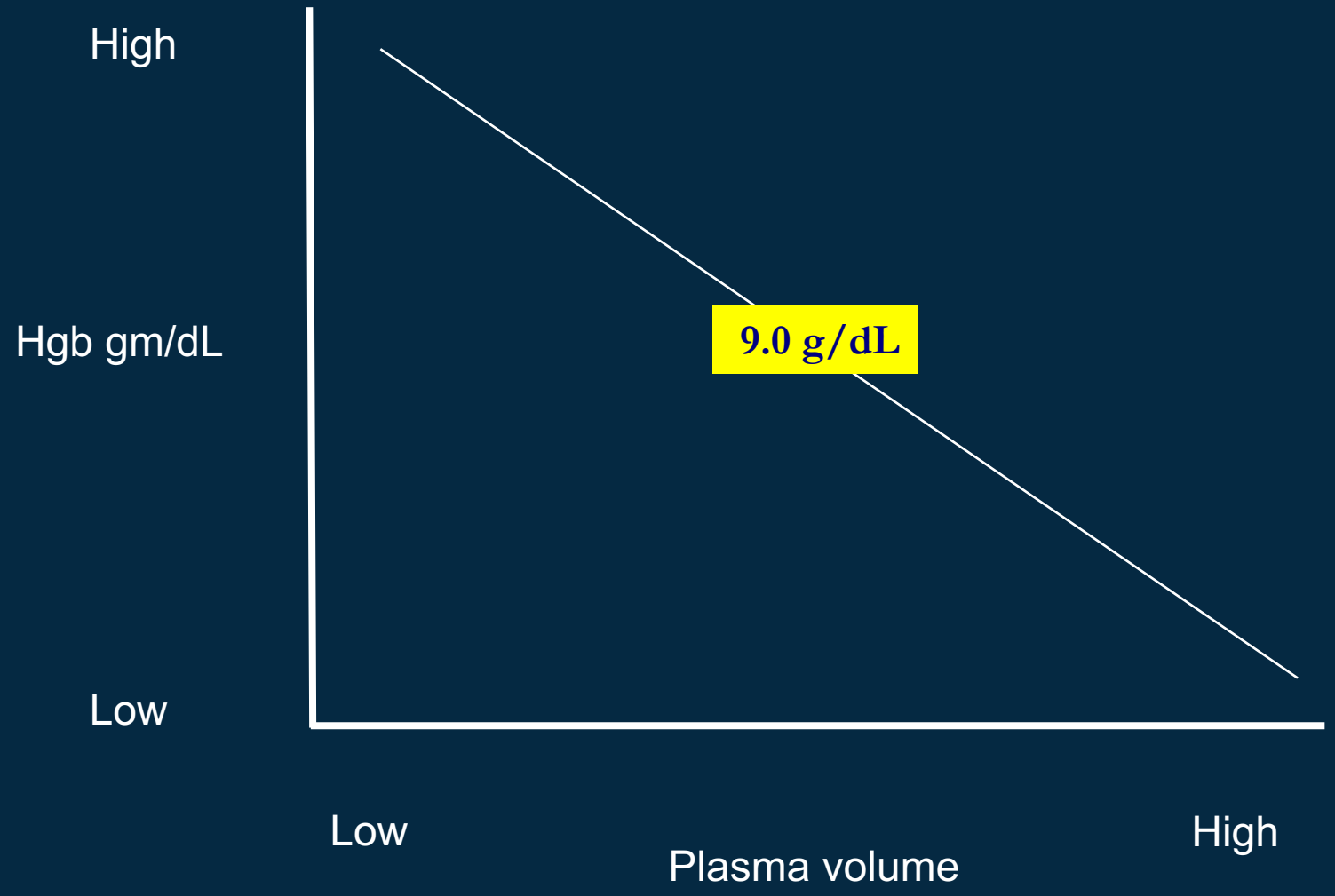
MALE

FEMALE

NORMAL RED CELL MASS



REDUCED RED CELL MASS



	Recommendations
NIH Consensus Conference,[42] 1988	<70 g/L (acute)
American College of Physicians,[43] 1992	No number
American Society of Anesthesiologists,[44] 1996	<60 g/L (acute)
American Society of Anesthesiologists,[45] 2006	No number
Canadian Medical Association,[26] 1997	No number
Canadian Medical Association,[46] 1998	No number
College of American Pathologists,[47] 1998	60 g/L (acute)
British Committee for Standards in Haematology,[48] 2001	No number
British Committee for Standards in Haematology,[49] 2012	70 g/L*
Australasian Society of Blood Transfusion,[50] 2001	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[51] 2007	70 g/L
Society for Thoracic Surgeons, Society of Cardiovascular Anesthesiology,[52] 2011	80 g/L*
American College of Critical Care Medicine, Society of Critical Care Medicine,[53] 2009	70 g/L
American College of Critical Care Medicine, Society of Critical Care Medicine,[54] 2009	70 g/L
Society for the Advancement of Blood Management,[55] 2011	80 g/L
National Blood Authority, Australia,[13] 2012	No number
AABB,[56] 2012	70–80 g/L or 80 g/L†
Kidney Disease: Improving Global Outcomes,[57] 2012	No number
National Cancer Center Network,[58] 2012	70 g/L

*For patients with acute blood loss. †For patients with symptoms of end-organ ischaemia.

Goodnough LT et.al. Lancet 2013

EJA

Eur J Anaesthesiol 2017; **34**:332–395

GUIDELINES

Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology

First update 2016

Sibylle A. Kozek-Langeneck
Guidrius Barauskas, Edoarc
Thorsten Haas, Matthias Jac
Jens Meier, Zsolt L. Molnar,
Philippe J.F. Van der Linden,

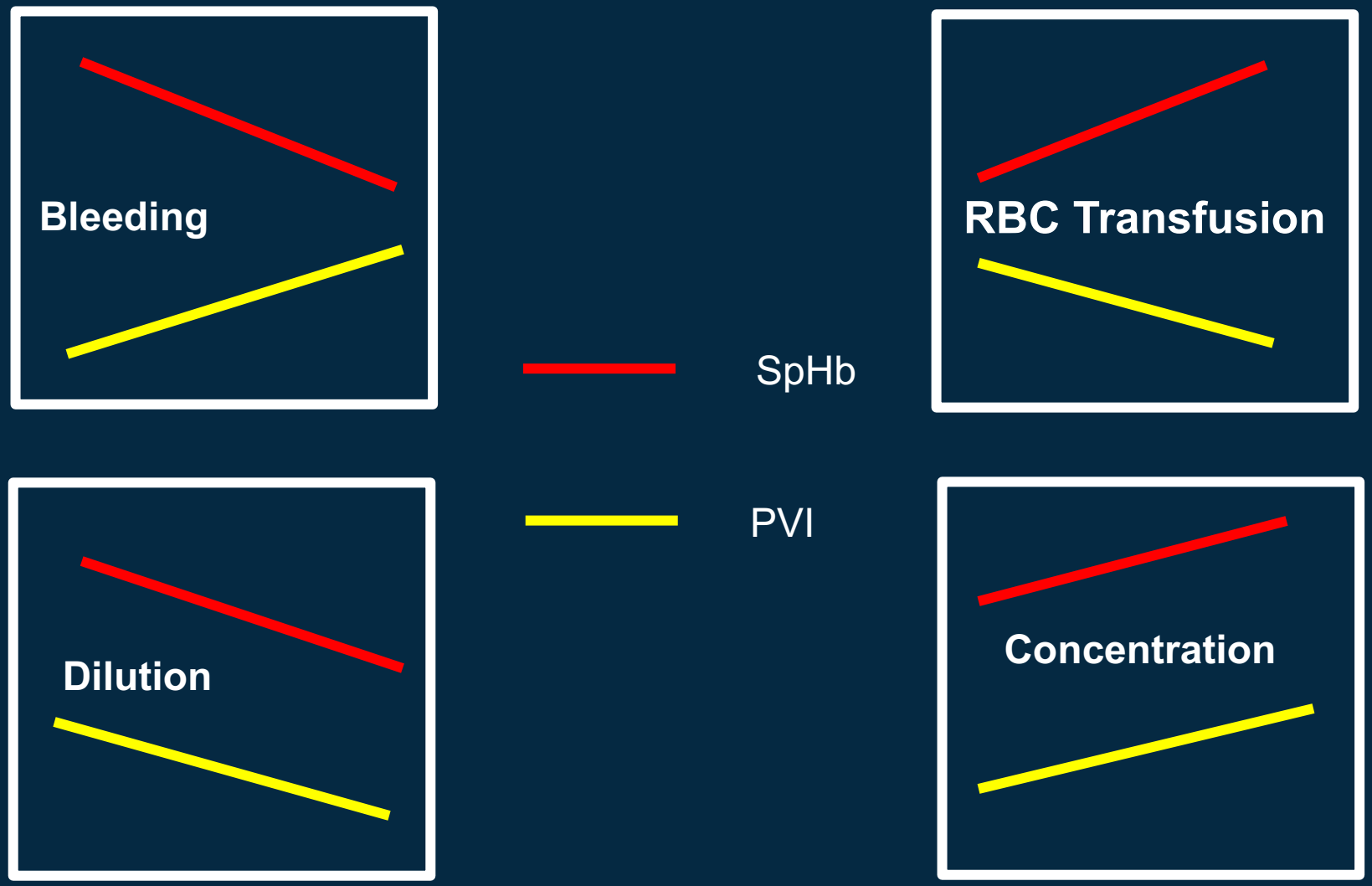
1.3.1. Transfusion triggers

We recommend a target haemoglobin concentration of 7 to 9 g dl^{-1} during active bleeding. **1C**

Continuous haemoglobin monitoring can be used as a trend monitor. **C**

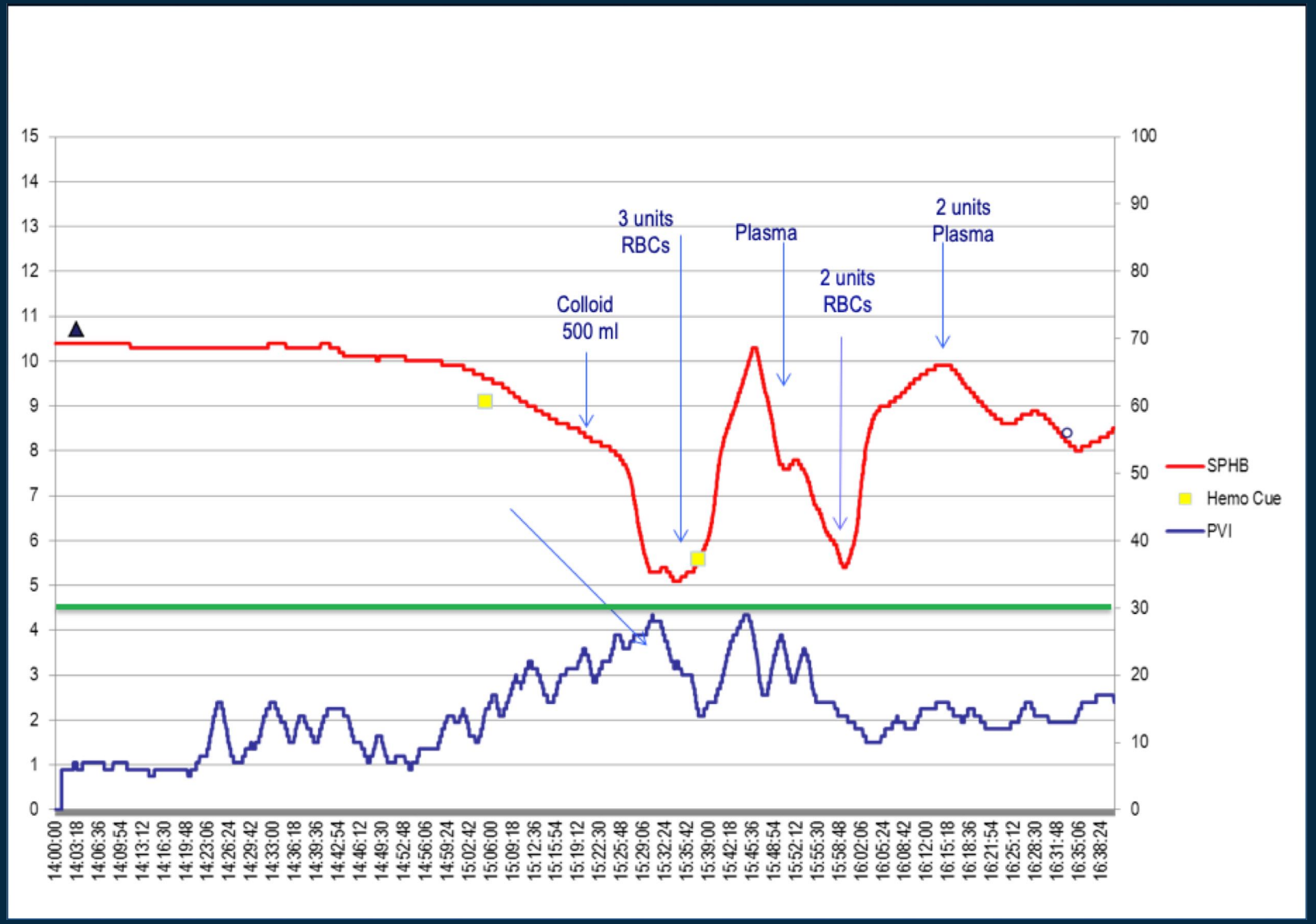

Masimo
7.0
17.0
7.0
SpHb
20
PVI
PI
74
3
15
9
7.0
1.0
Root
SpHb
PVI

RELATIONSHIP OF PVI AND SpHb



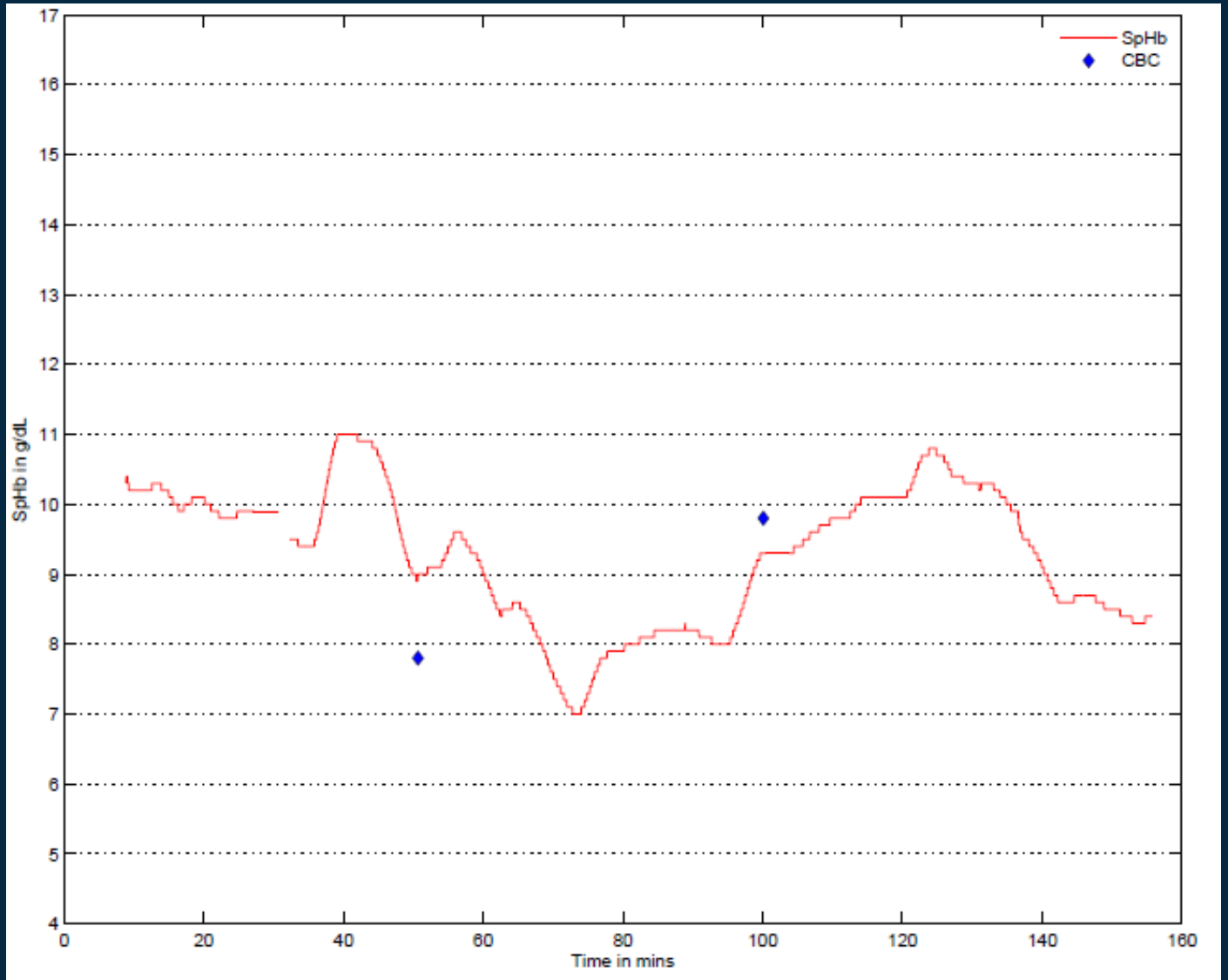
Shander A. with permission

BLEEDING IN SURGERY



POST-SURGICAL: CARDIAC ICU

Case Example



RED BLOOD CELL TRANSFUSION IN ADULT TRAUMA AND CRITICAL CARE

- Recommendations Regarding RBC Transfusion in Patients With Neurologic Injury and Diseases

✔ **Level 1**

- There are insufficient data to support level I recommendations on this topic.

✔ **Level 2**

- There is no benefit of a “liberal” transfusion strategy (transfusion when Hb < 10 g/dL) in patients with moderate to severe traumatic brain injury.

✔ **Level 3**

- Decisions regarding blood transfusion in patients with subarachnoid hemorrhage must **be assessed individually** **because optimal transfusion triggers are not known** and there is no clear evidence that blood transfusion is associated with improved outcome.

CCM 2009 and J. Trauma 2009

ORIGINAL RESEARCH ARTICLE Open Access

Physicians' lack of knowledge - a possible reason for red blood cell transfusion overuse?

Roni Rahav Koren[1,3*], Celia Suriu[1,2], Orly Yakir[1,2], Luiza Akria[1,2], Masad Barhoum[1,2†] and Andrei Braester[1,2†]

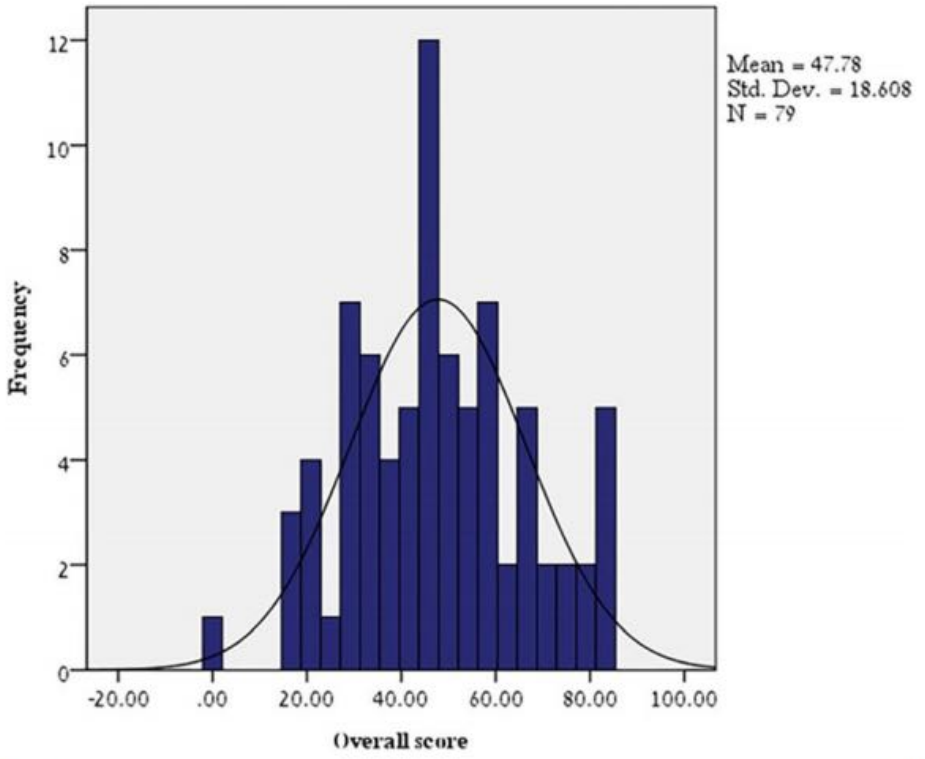


Fig. 1 Scores of the overall questionnaire. Distribution of the overall knowledge scores of the study population. Mean overall knowledge score of the population study was 47.8 ± 18.6

Overall average knowledge score: 47.8

Isr J Health Policy Res. 2017

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Annals of Internal Medicine

EDITORIAL

From Tolerating Anemia to Treating Anemia

Transfusion trials undoubtedly have transformed our view of the role of allogeneic blood in patient care, leading to a welcome shift toward reduced use of allogeneic red blood cell (RBC) transfusion. Nonetheless, this change arguably has also given rise to unintended consequences. As the name implies, a transfusion trial stays focused on comparing different transfusion strategies while placing the alternatives for managing anemia on the so-called back burner (1).

2019 Shander A et.al.

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

Lars B. Holst, M.D., Nicolai Haase, M.D., Ph.D., Jørn Wetterslev, M.D., Ph.D., Jan Wernerman, M.D., Ph.D., Anne B. Guttormsen, M.D., Ph.D., Sari Karlsson, M.D., Ph.D., Pär I. Johansson, M.D., Ph.D., Anders Åneman, M.D., Ph.D., Marianne L. Vang, M.D., Robert Winding, M.D., Lars Nebrich, M.D., Helle L. Nibro, M.D., Ph.D., Bodil S. Rasmussen, M.D., Ph.D., Johnny R.M. Lauridsen, M.D., Jane S. Nielsen, M.D., Anders Oldner, M.D., Ph.D., Ville Pettilä, M.D., Ph.D., Maria B. Cronhjort, M.D., Lasse H. Andersen, M.D., Ulf G. Pedersen M.D., Nanna Reiter, M.D., Jørgen Wiis, M.D., Jonathan O. White, M.D., Lene Russell, M.D., Klaus J. Thornberg, M.D., Peter B. Hjortrup, M.D., Rasmus G. Müller, M.D., Morten H. Møller, M.D., Ph.D., Morten Steensen, M.D., Inga Tjäder, M.D., Ph.D., Kristina Kilsand, R.N., Suzanne Odeberg-Wernerman, M.D., Ph.D., Brit Sjøbø, R.N., Helle Bundgaard, M.D., Ph.D., Maria A. Thyø, M.D., David Lodahl, M.D., Rikke Mærkedahl, M.D., Carsten Albeck, M.D., Dorte Illum, M.D., Mary Kruse, M.D., Per Winkel, M.D., D.M.Sci., and Anders Perner, M.D., Ph.D., for the TRISS Trial Group* and the Scandinavian Critical Care Trials Group

TRISS Trial

PRIMARY AND SECONDARY OUTCOME MEASURES

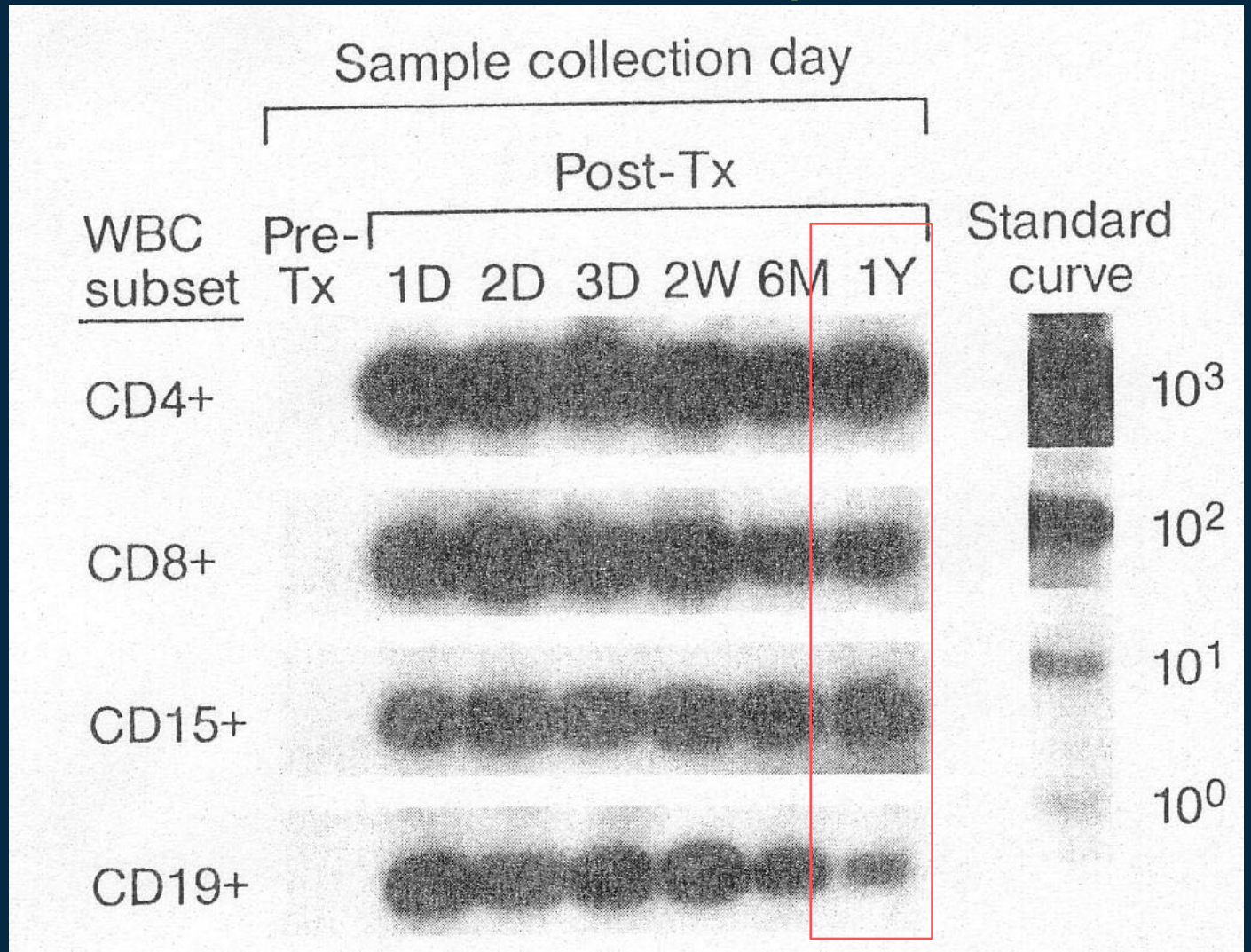
Outcome	Lower Hemoglobin Threshold	Higher Hemoglobin Threshold	Relative R… (95…	P Value
Primary outcome: death by day 90 — no./total no. (%)	216/502 (43.0)	223/496 (45.0)		0.44†
Secondary outcomes‡				
Use of life support — no./total no. (%)§				
At day 5	278/432 (64.4)		1.04 (0.93–1.14)	0.47†
At day 14	140/380 (…)	…8)	0.99 (0.81–1.19)	0.95†
At day 28		…4/322 (19.9)	0.77 (0.54–1.09)	0.14†
Ischemic event in the ICU — no./total no. (%)¶		39/489 (8.0)	0.90 (0.58–1.39)	0.64
Severe adverse reaction — no./total n…		1/489 (0.2)	—	1.00
Alive without vasopressor or i… mean % of days**	73	75	—	0.93
Alive without m… …ean % of …	65	67	—	0.49
Al… …ient therapy — mean %	85	83	—	0.54
… of the hospital — mean % of days††	30	31	—	0.89

More Than 10-20 Times Normal

Holst LB et al. N Engl J Med. 2014

GENE TRANSFER

Quantitative allele-specific PCR

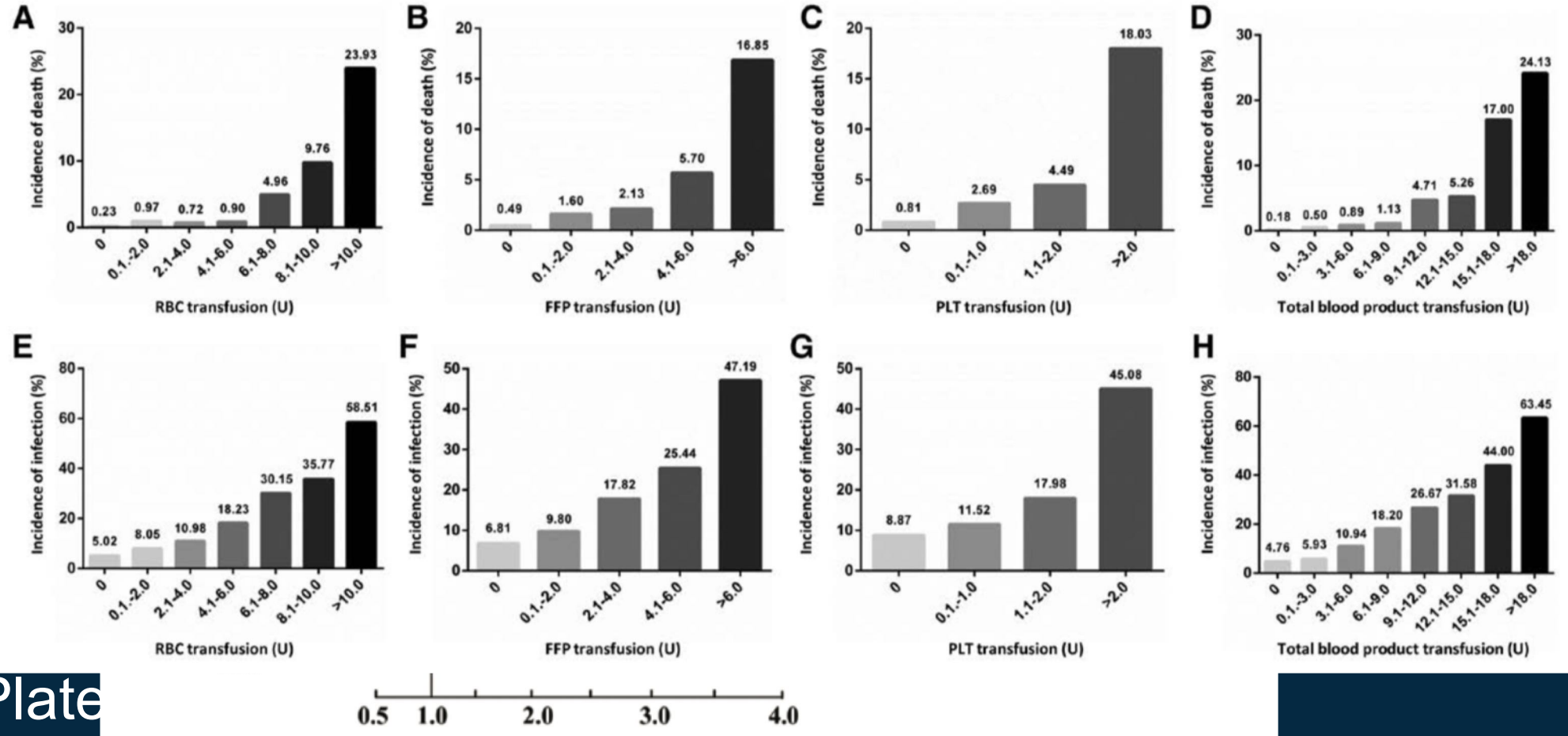


Blood *1999;93:3127*

GENE TRANSFER WITH TRANSFUSION

Nevada man's DNA changes after bone marrow transplant and is replaced by that of his German donor following treatment for leukemia

Transfusion of Red Blood Cells, Fresh Frozen Plasma, or Plat tion After (



Plate

A&A epub 2019

TRANSFUSION AS THERAPY

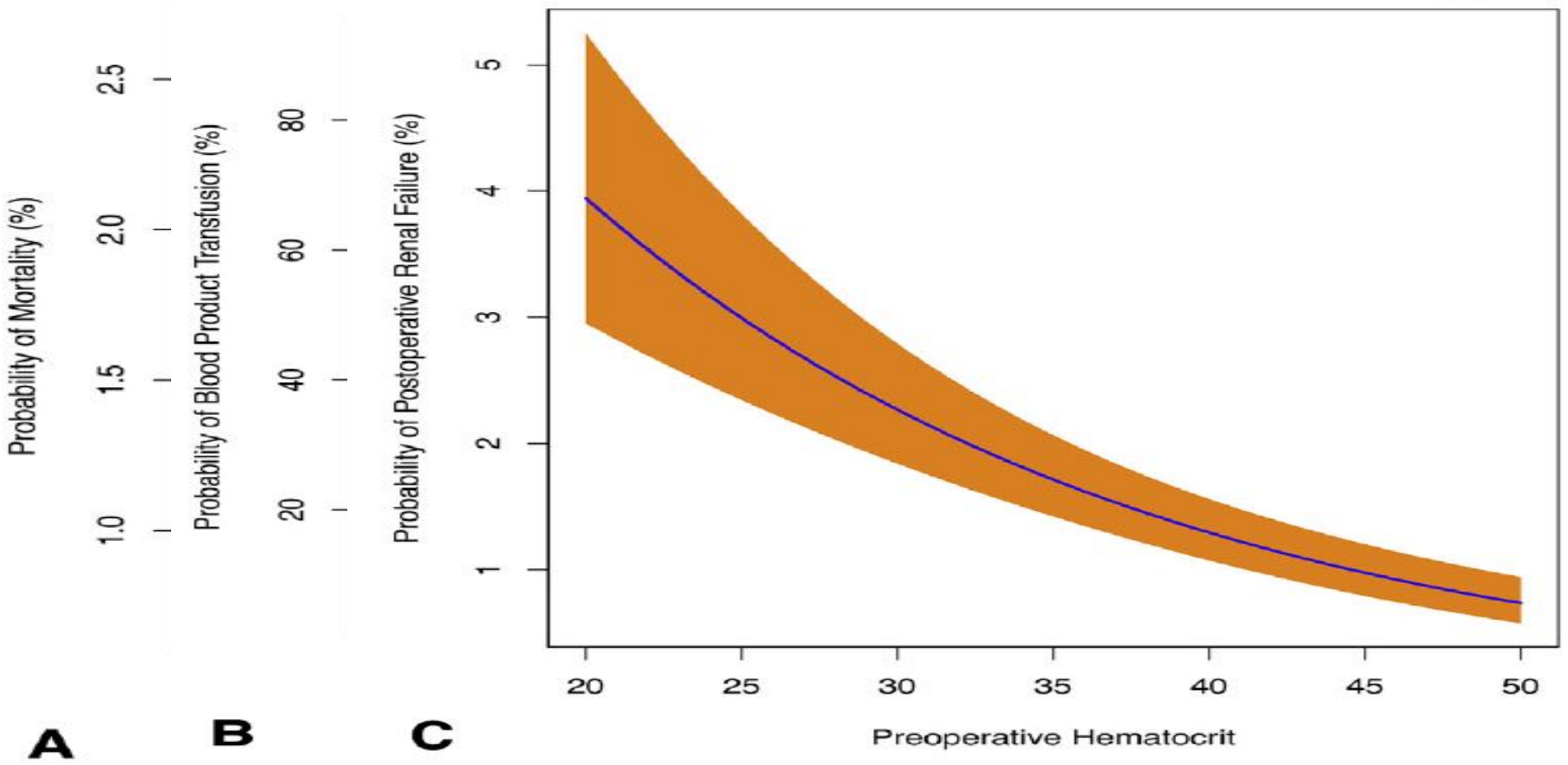
Blood Shield Laws

- Blood is “unavoidably unsafe”
- Blood is “inherently dangerous”

Zuck TF Arch Pathol Lab Med 1990;114:309-315

Preoperative anemia versus blood transfusion: Which is the culprit for worse outcomes in cardiac surgery?

Damien J. LaPar, MD, MSc,[a] Robert B. Hawkins, MD, MSc,[a] Timothy L. McMurry, PhD,[a]
James M. Isbell, MD, MSCI,[a] Jeffrey B. Rich, MD,[b] Alan M. Speir, MD,[c] Mohammed A. Quader, MD,[d]



J Thorac Cardiovasc Surg. 2018

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1

Don't transfuse more units of blood than absolutely necessary.

Each unit of blood carries risks. A restrictive threshold (7.0-8.0g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation (evidence supports a threshold of 8.0g/dL in patients with pre-existing cardiovascular disease). Transfusion decisions should be influenced by symptoms and hemoglobin concentration. Single unit red cell transfusions should be the standard for non-bleeding, hospitalized patients. Additional units should only be prescribed after re-assessment of the patient and their hemoglobin value.

MAZER VS. MURPHY

- Looking beyond txn as the "only treatment option"
  - What is the medical condition to diagnose here?
  - Are we managing that medical condition properly?

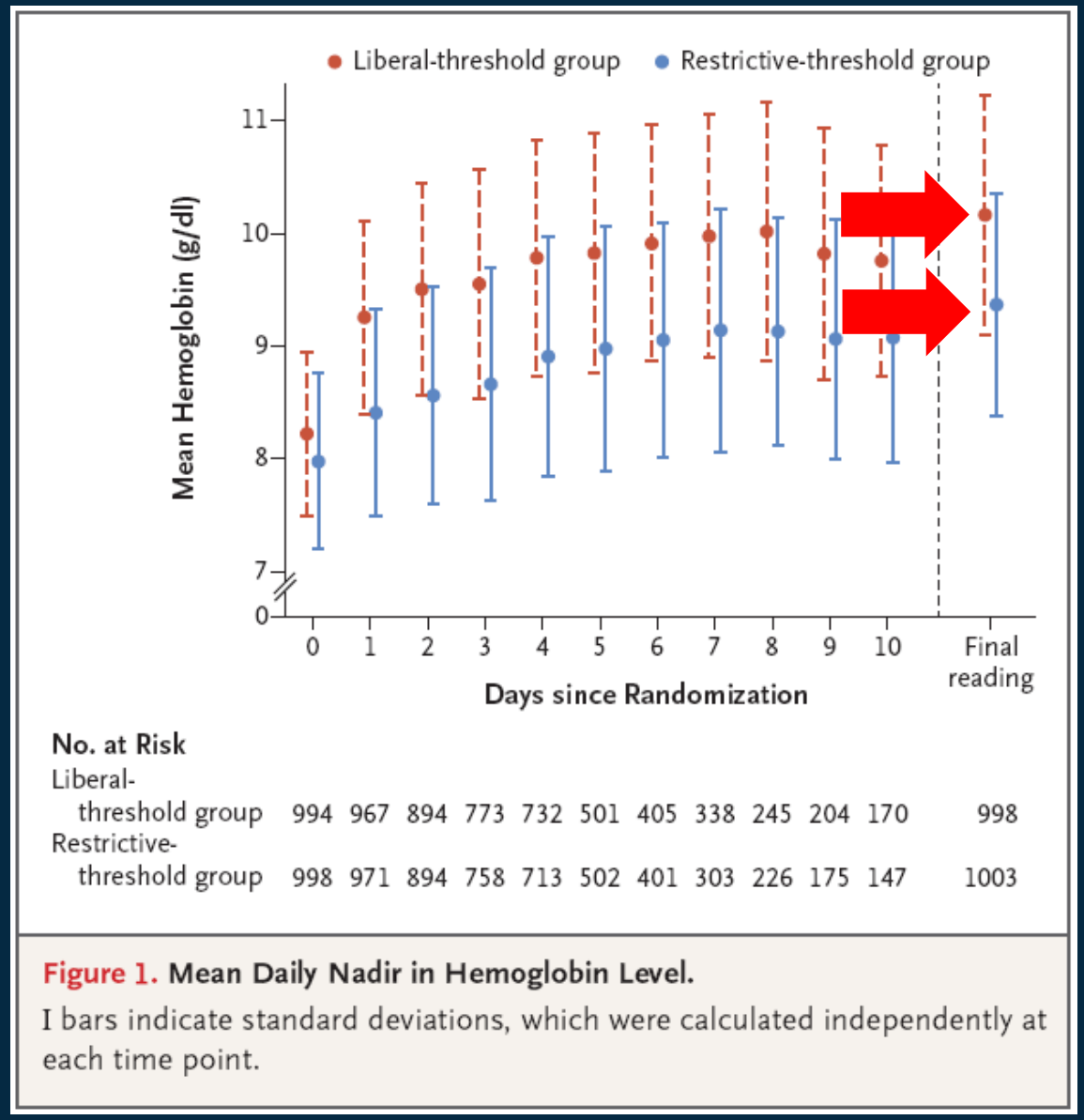

Figure 1. Mean Daily Nadir in Hemoglobin Level.

I bars indicate standard deviations, which were calculated independently at each time point.

Murphy et al. NEJM 2015

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ISBT International Society of Blood Transfusion

Blood transfusion: one unit too much or one unit [illegible] – which strategy poses the smallest risk to the

E. Seifried & M. M. Mueller

Risk? What about benefit?

The best transfusion strate[illegible]optimal dosing for packed red blood cells are still mi[illegible]**st indications**. Sufficiently powered, prospe[illegible]omized, controlled clinical transfusion trials for pa[illegible]lood cells in most clinical settings are **urgen[illegible]d to reduce ill-founded clinical decisions and to base[illegible]lusion strategies on clinical evidence and scientific study results.**

2018

PREVALENCE OF IRON DEFICIENCY ANEMIA

- Walsh TS et al. - 35% of patients have red cell indices consistent with functional iron deficiency at ICU admission[1]
- Lasocki S et al. Iron deficiency may affect up to 40% of critically ill patients [2]
- Rodriguez RM et. al. 9% of ICU patients were iron deficient, 2% B12 deficient, and 2% folic acid deficient[3]

1. Walsh TS. Br J Anaesth. 2006
2. Lasocki S. Anesthesiology, 2011
3. Rodriguez RM . J Crit Care. 2001

Prevalence of iron deficiency on ICU discharge and its relation with fatigue: a multicenter prospective study

Sigismond Lasocki[1,6*], Nicolas Chudeau[1], Thibaut Papet[2], Deborah Tartiere[3], Antoine Roquilly[4], Laurence Carlier[1], Olivier Mimoz[2], Philippe Seguin[3], Yannick Malledant[3], Karim Asehnoune[4], Jean François Hamel[5] and for the AtlanREA group

- The prevalence of ID was approximately 10% on ICU discharge
- The prevalence of ID increased to 35% at 6 months
- A quarter of the critically ill patients were still anemic at 6 months
- ID was associated with increased fatigue 1 month after ICU discharge, independently of low Hb levels

Crit Care. 2014

ANEMIA PREVALENCE

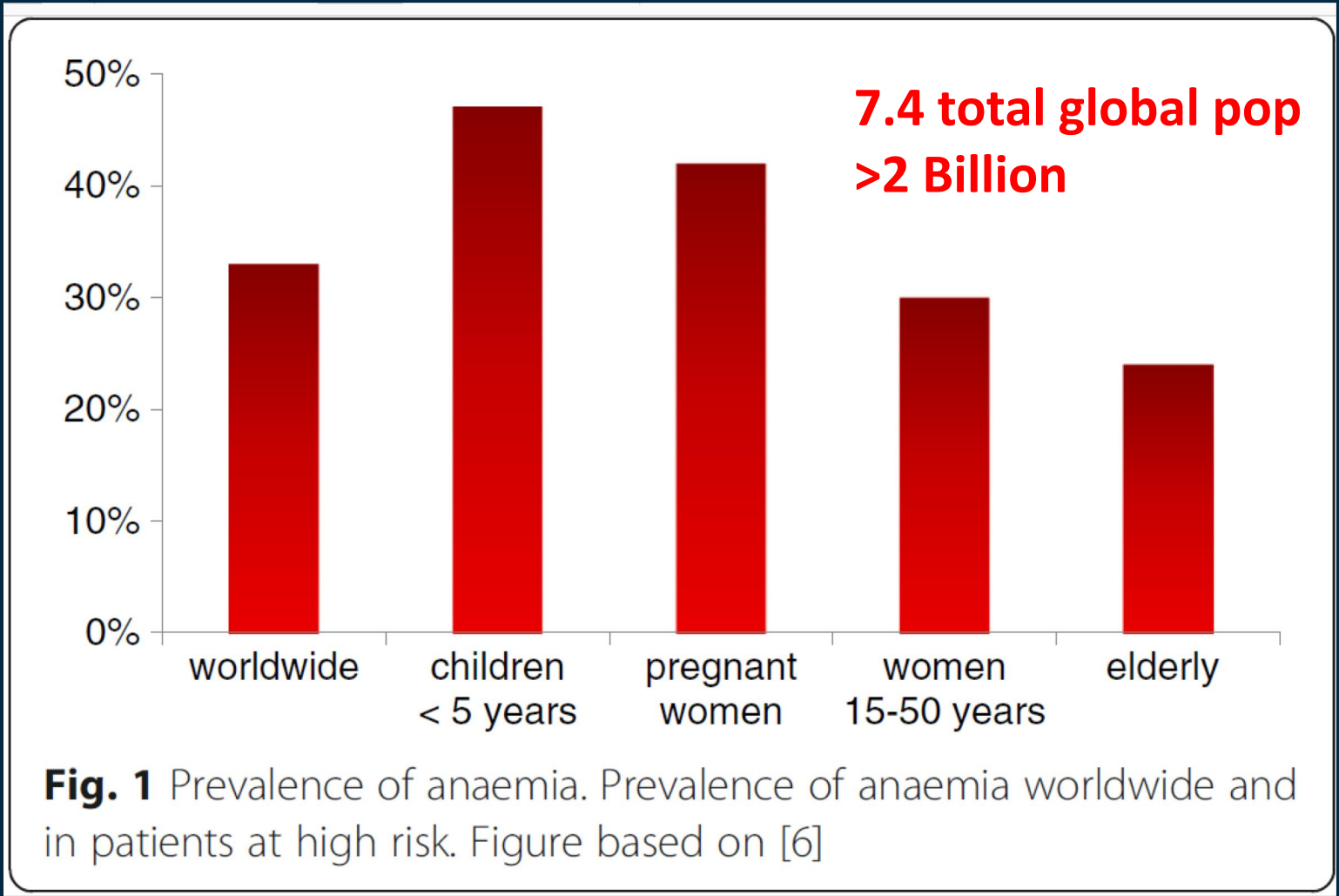

Fig. 1 Prevalence of anaemia. Prevalence of anaemia worldwide and in patients at high risk. Figure based on [6]

Chandra et al. Critical Care 2017

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2

Don't transfuse red blood cells for iron deficiency without hemodynamic instability.

Blood transfusion has become a routine medical response despite cheaper and safer alternatives in some settings. Pre-operative patients with iron deficiency and patients with chronic iron deficiency without hemodynamic instability (even with low hemoglobin levels) should be given oral and/or intravenous iron.

Anemia in Critical Illness

Insights into Etiology, Consequences, and Management

Shailaja J. Hayden[1], Tyler J. Albert[1,2], Timothy R. Watkins[1,3], and Erik R. Swenson[1,2]

- Anemia is highly prevalent in the critically ill
- It is associated with higher health care resource use
- Associated with poor patient outcomes
- Further research should delineate risks, benefits, and effectiveness of various management strategies in specific patient populations rather than transfusion triggers

Am J Respir Crit Care Med. 2012

ETIOLOGY OF ANEMIA IN THE CRITICALLY ILL

- Diagnostic phlebotomy (~ 750-900 mL/ICU stay)
  - Range 40-80 mL/day
  - Accounts for 20% of total blood loss
- Occult and overt bleeding: wounds, drains & GI tract
- Anemia due to underproduction*
  - Blunted erythropoietin response to low Hct
  - Cytokines (IL-1b, TNF-a) inhibit erythropoietin gene
  - Inflammatory processes in the ICU - Hepcidin
  - Altered iron metabolism
  - Impaired proliferation and differentiation of erythroid progenitors
- Hemodilution?

Smoller BR, et al. *N Engl J Med*. 1986;314:1233-1235
Corwin HL, et al. *Chest*. 1995;108:767-771.
von Ahsen N, et al. *Crit Care Med*. 1999;27:2630-2639.
Corwin HL, et al. *Crit Care Med*. 2000;28:3098-3099.

“THERE IS NO REMEDY IN THE WORLD WHICH WORKS AS MANY MIRACLES AS BLEEDING.”

Guy Patin 1645

PHLEBOTOMY IN ICU AND NON ICU PATIENTS

- 50 ward patients, 50 all or part of hospitalization in ICU
- Ward - samples 1.1/day, mean 12.4 ml/day, 175 ml
- ICU - samples 3.4/day, mean 41.5 ml/day, 762 ml
- If had a-line more blood draws and more blood drawn
- 56% ICU patients transfused vs 16% Ward patients
- 50% of transfused had phlebotomy > 180 ml

Smoller & Kruskall *NEJM* 1986

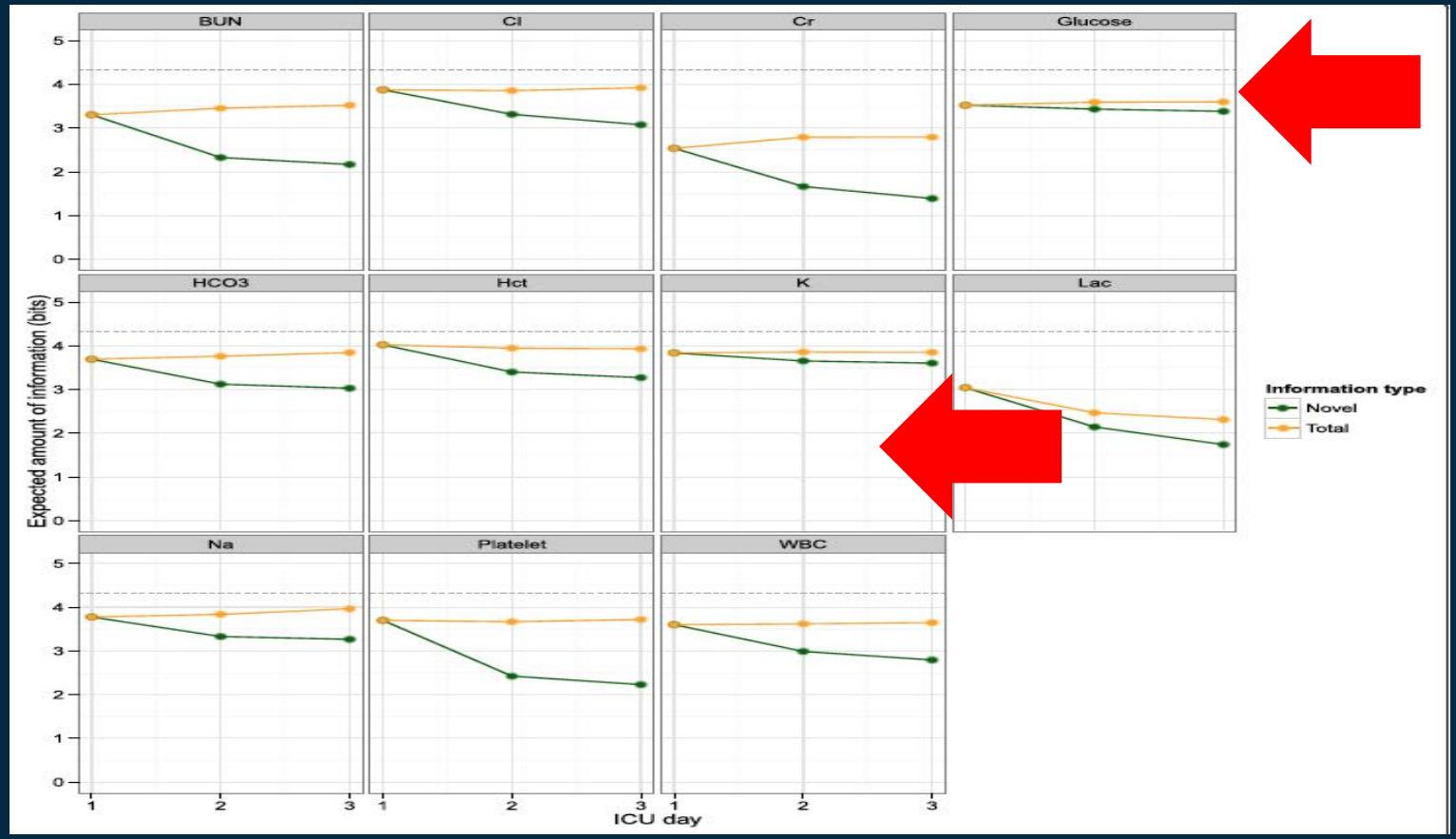
PHLEBOTOMY

- “In today’s medicine blood letting continues … unabated. We have refined the technique, call it ‘lab work‘ jab the patient incessantly, generate reams of questionable data ...”

Rosenzweig *Arch Intern Med* 1978

UNNECESSARY LAB TESTS

- Information theory to identify redundancy in common lab tests



Lee & Maslov *Int BMC Med Informatics Decision Making* 2015

REDUCING PHLEBOTOMY

- Strategy
  - Low volume blood tubes
  - Standardization of blood collection from central lines
  - POC glucose testing
- Average daily blood loss reduction per ICU patient of 10 ml
- Reduction of RBC transfusion of 15%

Coene et al *J Thromb Haemost* 2015

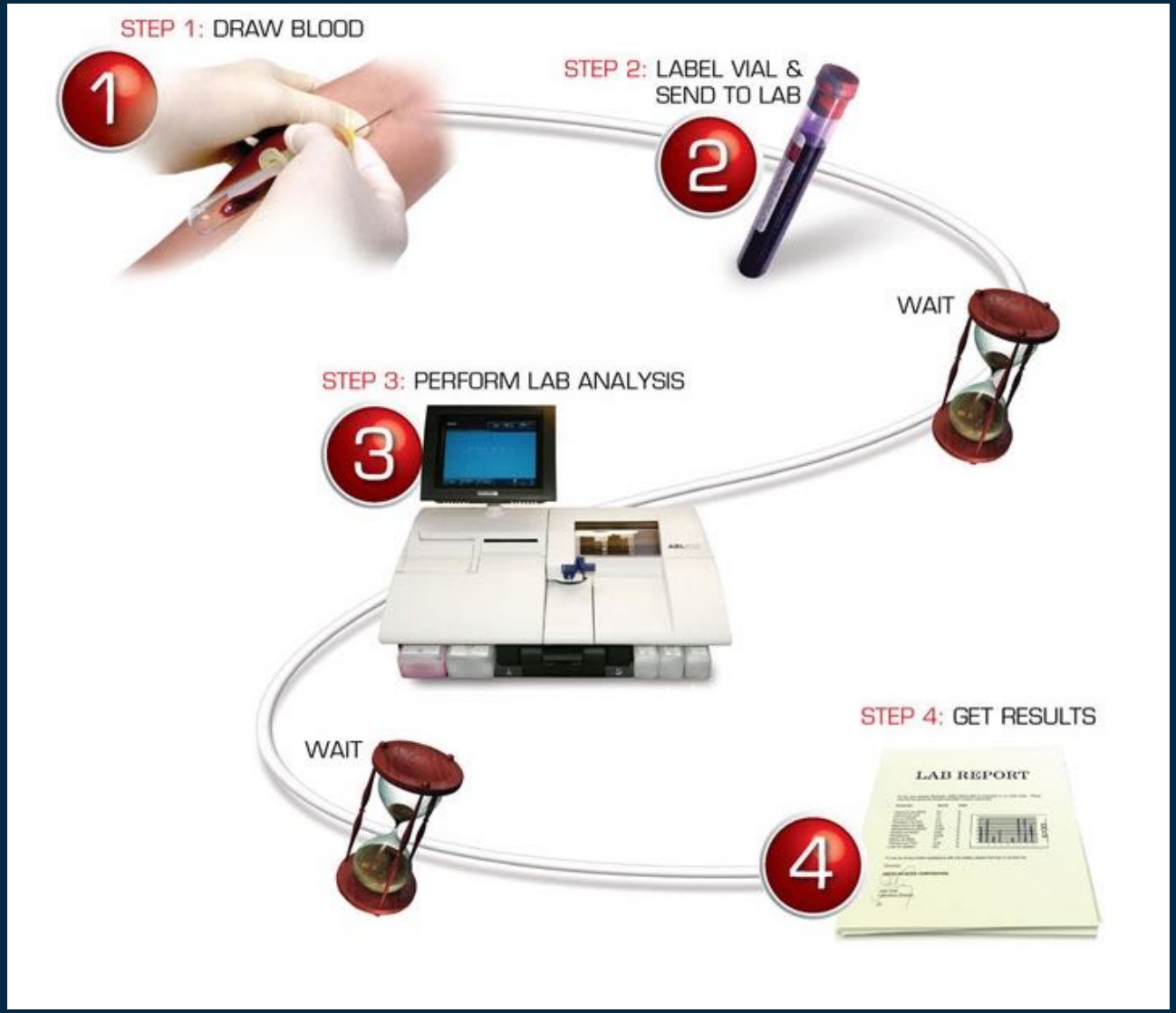
Twenty-five million liters of blood into the sewer

M. LEVI

- Current collection methods and the small amounts of blood or serum required by modern laboratory analyzers:
  - Each 25 million liter of patients' blood is thrown into waste containers
- 4 times more than the total volume of blood that is transfused each year
- Patients develop ‘HAA' due to blood collection
  - Associated with an adverse outcome
- Collection methods - adapted to the much smaller volumes required by new generation laboratory analyzers
  - Especially for hematology or oncology patients, critically ill patients, or children

J Thromb Haemost. 2014

LAB Hb: INTERMITTENT & DELAYED RESULTS TRANSFUSION DECISIONS MADE IN REAL TIME



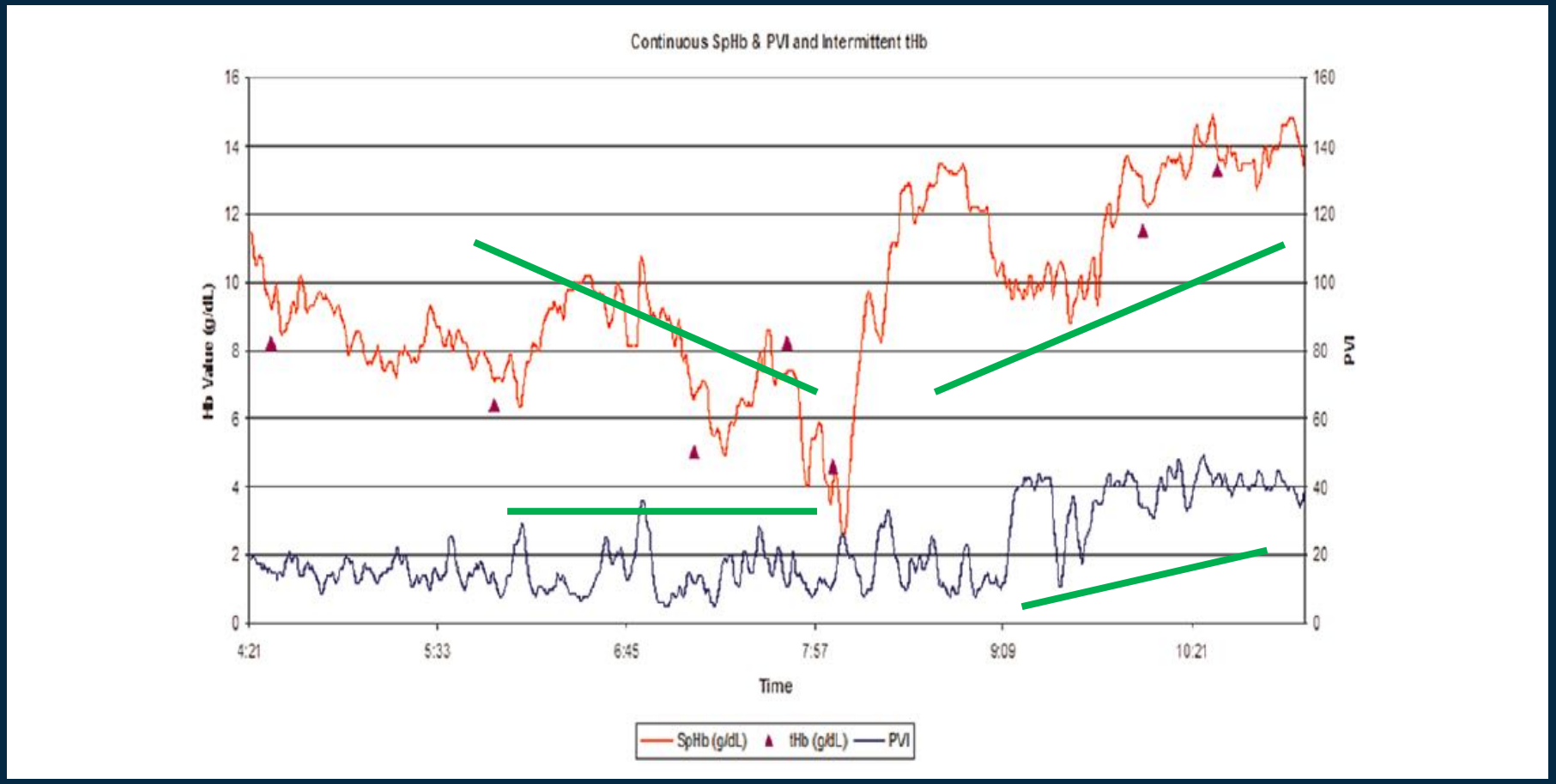

Masimo
7.0
17.0
7.0
SpHb
20
PVI
12.0
PI
74
3
15
9
7.0
1.0
Root
SpHb

SABM

Continuous Noninvasive Hemoglobin Monitoring: A Measured Response to a Critical Review

Steven J. Barker, PhD, MD,* Aryeh Shander, MD,†‡ and Michael A. Ramsay, MD§

SpHb and Bleeding: An example



A&A 2016

Accurate to 1 cm

Accurate to 1 meter

Which one is preferred?

Accuracy over reliability?

Journal of Clinical Monitoring and Computing 2016 end of year summary: cardiovascular and hemodynamic monitoring

Bernd Saugel[1] · Karim Bendjelid[2] · Lester A. Critchley[3] · Steffen Rex[4] · Thomas W. L. Scheeren[5]

9 Hemodynamic monitoring: impact on patient outcome and clinical decision-making

As hemodynamic monitoring can only improve patient outcome if coupled with therapeutic interventions the JCMC welcomes studies investigating the impact of hemodynamic management on clinical decision-making and outcome.

J Clin Monit Comput 2017

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4

Don't perform serial blood counts on clinically stable patients.

Transfusion of red blood cells or platelets should be based on the first laboratory value of the day unless the patient is bleeding or otherwise unstable. Multiple blood draws to recheck whether a patient's parameter has fallen below the transfusion threshold (or unnecessary blood draws for other laboratory tests) can lead to excessive phlebotomy and unnecessary transfusions.

PHLEBOTOMY TEST TUBES

Ranasinghe T.et al. Br J Haematol. 2013

CLINICAL STRATEGIES TREATING ANEMIA

- Early identification & treatment of anemia before reaching a “Transfusion Threshold (TRIGGER)”
- Avoid daily blood draws unless absolutely needed
- Use of other treatments before allogeneic blood
  - ESA
- Nutritional supplements
  - **Iron and possible hepcidin antagonists**
  - Folic Acid
  - B_{12}
- Bleeding and BM failure, directed therapy

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Patient Blood Management in the Intensive Care Unit

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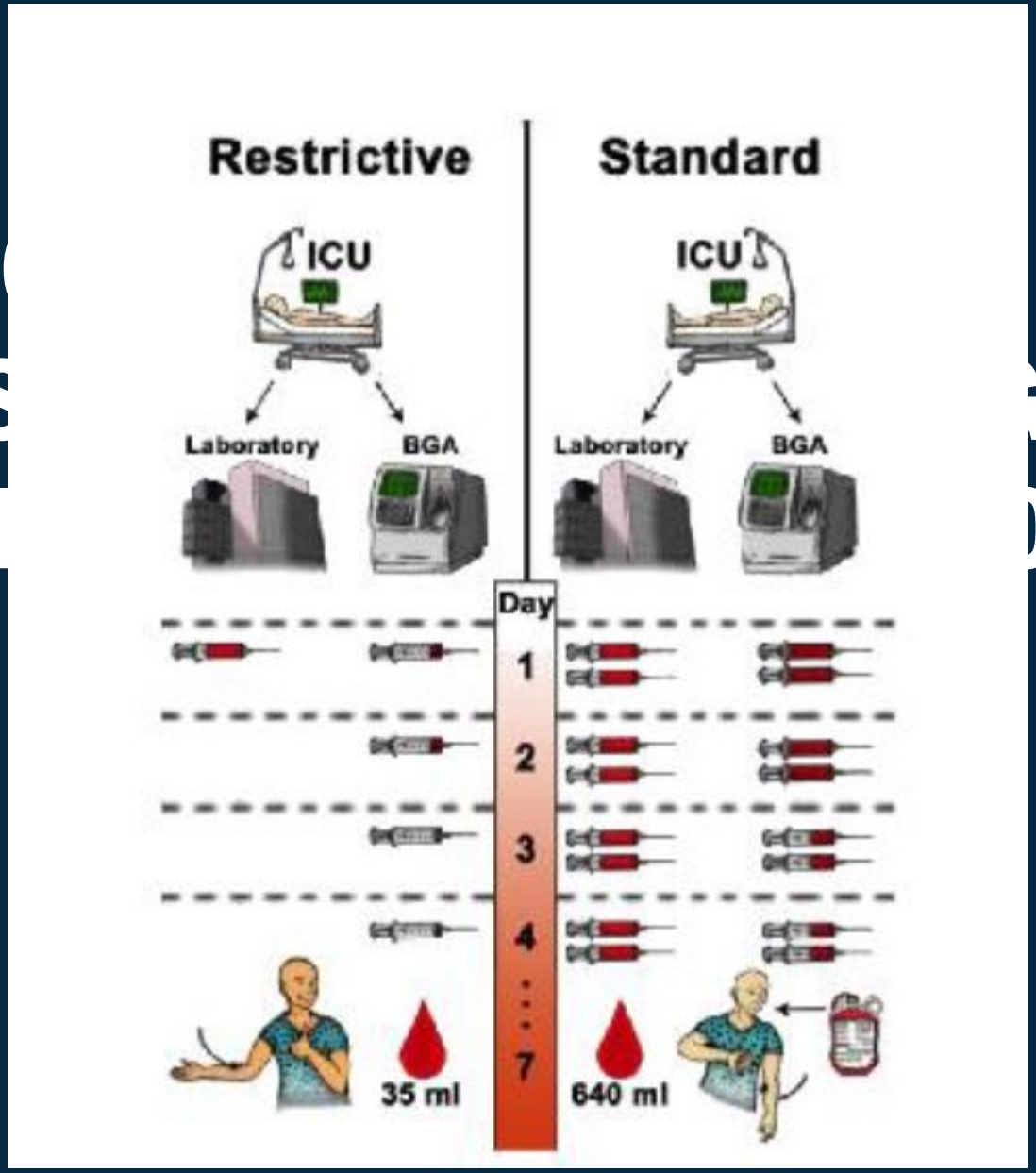
THE FRE OF DIAGNOSTIC BLOOD S GHT) AND AFTER (LEFT) TI OF PBM



Meybohm P et al. J Cardiothorac Vasc Anesth. 2019

Perel *Critical Care* (2017) 21:291
DOI 10.1186/s13054-017-1872-1

Critical Care

EDITORIAL Open Access

Iatrogenic hemodilution: a possible cause for avoidable blood transfusions?

Azriel Perel

2017

Continuous Noninvasive Hemoglobin Monitoring

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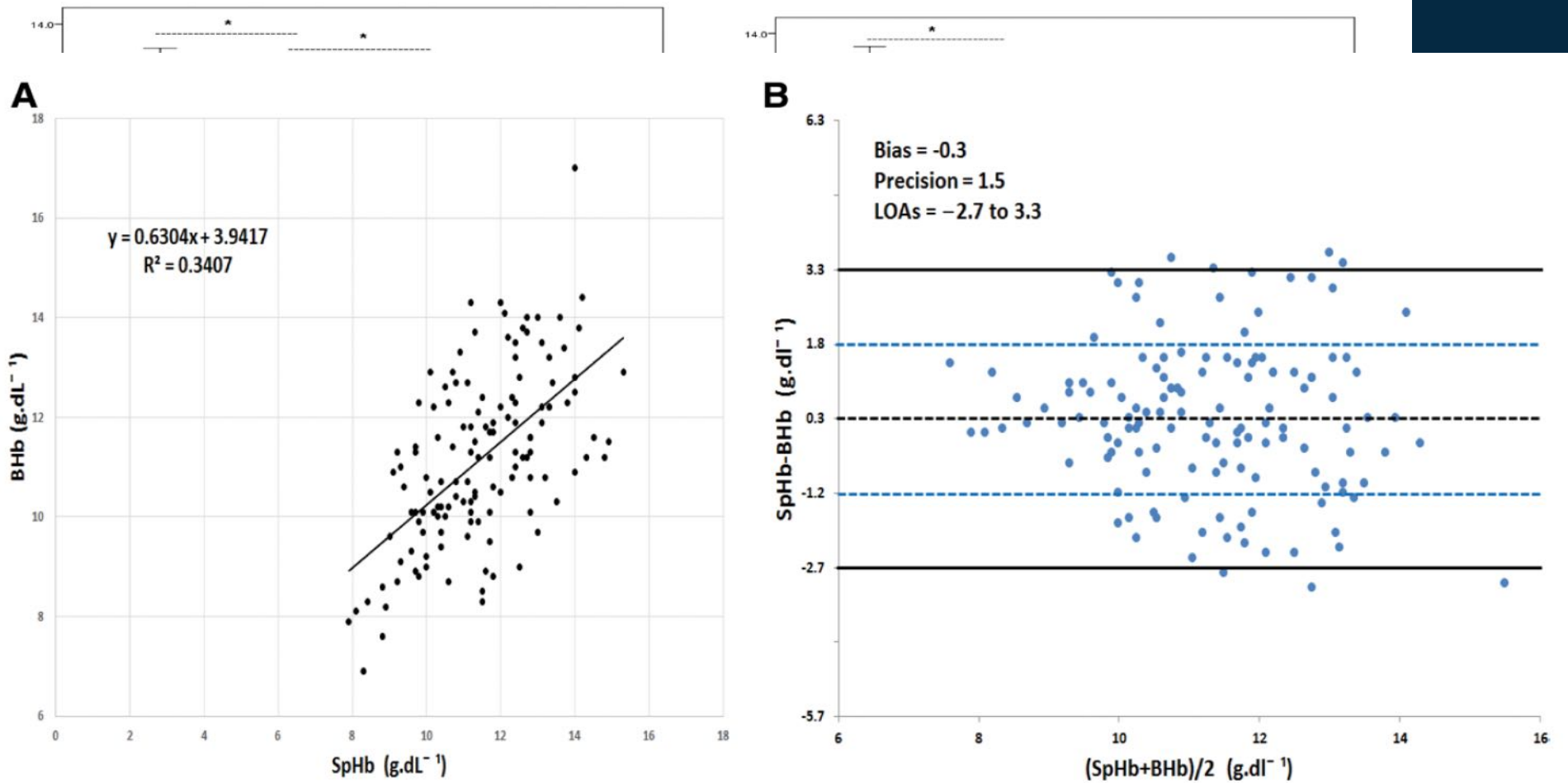

Figure 2. A, A scatter plot of 132 paired measurements as determined by BHb and by SpHb. SpHb and BHb are expressed as g/dL. The correlation coefficient (*r*) was 0.58, and the 95% confidence interval was 0.46–0.68. B, Corrected Bland–Altman plot for repeated measurements of 132 paired hemoglobin values as determined by BHb and by SpHb. The dashed black line represents the mean bias (−0.3 g·dL^{-1}), the dashed blue lines represent 1 SD (1.5 g·dL^{-1}), and the continuous black lines represent the LOA (−2.7 to 3.3 g·dL^{-1}). BHb indicates laboratory hemoglobin; LOA, limit of agreement; SD, standard deviation; SpHb, continuous noninvasive hemoglobin.

Patient Blood Management

What Else ?

TABLE 1. Benefits of Patient Blood Management

	Change	*P*	Number of Patients

Now that safety and efficacy of patient blood management has systematically been confirmed by this meta-analysis, the stage is set for worldwide implementation. Conversely, not implementing patient blood management represents substandard care.

LOS indicates length of stay.

Ann Surg. 2019

SABM

Patient blood management is not about blood transfusion: it is about patients' outcome

BLOOD TRANSFUSION

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We have sincere concerns that the organizers of the conference (i.e. blood establishment) might (should) not be in the best position to publish recommendations for the use of their "products" free of conflicts of interest.

SUMMARY

- Why PBM in the ICU?
- Prevalence of anemia in ICU
- Consequences of anemia
- Anemia causes (Etiology in critically ill patients)
- “New” concept of iatrogenic anemia
- Hemoglobin: Treating numbers vs. patients
- Hemoglobin monitoring
- The long-debated issue of accuracy
- Incorporating SpHb as part of PBM in the ICU

FOR MORE INFORMATION, GO TO: SABM.ORG