Anesthesia & Analgesia Journal Publish Ahead of Print

DOI: 10.1213/ANE.0000000000004844

The Essential Role of Patient Blood Management in a Pandemic: A Call for Action

Aryeh Shander, MD,[1] Susan Marie Goobie, MD,[2] Matthew A Warner, MD,[3] Matti Aapro, MD,[4] Elvira Bisbe, MD, PhD,[5] Angel A Perez-Calatayud, MD,[6] Jeannie Callum, MD,[7] Melissa M Cushing, MD,[8] Wayne B Dyer, PhD,[9] Jochen Erhard, MD,[10] David Faraoni, MD, PhD,[11] Shannon Farmer,[12] Tatyana Fedorova, PhD,[13] Steven M Frank, MD,[14] Bernd Froessler, MD, PhD,[15] Hans Gombotz, MD,[16] Irwin Gross, MD,[17] Nicole R Guinn, MD,[18] Thorsten Haas, MD,[19] Jeffrey Hamdorf, MD, PhD,[20] James P Isbister, MD,[21] Mazyar Javidroozi, MD, PhD,[1] Hongwen Ji, MD,[22] Young-Woo Kim, MD,[23] Daryl J Kor, MD,[24] Johann Kurz, PhD,[25] Sigismond Lasocki, MD, PhD,[26] Michael F Leahy, MBChB,[27] Cheuk-Kwong Lee, MD,[28] Jeong Jae Lee, MD, PhD,[29] Vernon Louw, MBChB, PhD,[30] Jens Meier, MD,[31] Anna Mezzacasa, PhD,[32] Manuel Munoz, MD, PhD,[33] Sherri Ozawa, RN,[34] Marco Pavesi, MD,[35] Nina Shander, BS,[36] Donat R Spahn, MD,[37] Bruce D Spiess, MD,[38] Jackie Thomson, MBChB,[39] Kevin Trentino, MPH,[40] Christoph Zenger, PhD,[41] and Axel Hofmann, Dr.rer.medic[42] on behalf of the International Foundation of Patient Blood Management (IFPBM) and Society for the Advancement of Blood Management (SABM) Work Group.

1) Department of Anesthesiology, Critical Care and Hyperbaric Medicine, Englewood Health, Englewood, NJ, USA

2) Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Harvard Medical School, Boston MA, USA

3) Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA

4) Cancer Center Clinique Genolier, Genolier, Switzerland

5) Department of Anesthesiology, Perioperative Medicine Research Group, Hospital del Mar Medical Research Institute, IMIM, Barcelona, Spain

6) Department of Critical Care, Hospital General de Mexico Dr Eduardo Liceaga, Mexcio City, Mexico

7) Laboratory Medicine and Molecular Diagnostics, Sunnybrook Health Sciences Centre, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

8) Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, NewYork-Presbyterian Hospital, New York, NY, USA

9) Australian Red Cross Lifeblood and Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia

10) Department of Surgery, Evangelisches Klinikum Niederrhein, Duisburg, Germany

11) Department of Anesthesiology and Pain Medicine, University of Toronto, The Hospital for Sick Children, Toronto, ON, Canada

12) Medical School and Division of Surgery, Faculty of Health and Medical Sciences, The University of Western Australia, Perth, Western Australia; and School of Health Sciences and Graduate Studies, Faculty of Health Sciences, Curtin University, Perth, Western Australia

13) Institute of Anesthesiology, Resuscitation and Transfusiology of the National Medical Research Center of Obstetrics, Gynecology and Perinatology named after Acad. V. I. Kulakov, Ministry of health of the Russian Federation, Moscow

14) Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland

15) Department of Anesthesia, Lyell McEwin Hospital, Elizabeth Vale, SA, Australia; Discipline of Acute Care Medicine, University of Adelaide, Adelaide, SA, Australia

16) Department of Anesthesiology and Intensive Care, General Hospital Linz, Austria

17) Northern Light Health, Maine, USA. Senior Medical Advisor, Accumen, Inc, USA

18) Department of Anesthesiology, Duke University Medical Center, Durham, NC, USA

19) Department of Anesthesiology, University Children's Hospital Zurich, Zurich, Switzerland

20) Medical School, The University of Western Australia, WA Patient Blood Management Group, Perth, Australia

21) Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia

22) Department of Anesthesiology and Transfusion Medicine, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

23) Department of Cancer Control and Population Health. National cancer Center Graduate School of Cancer Science and Policy & Center for Gastric Cancer, National Cancer Center, Ilsandonggu, Goyang, Korea

24) Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN, USA

25) Retired from the Austrian Federal Ministry of Health; University of Applied Sciences, Department Applied Sciences, Vienna, Austria

26) Département Anesthésie-Réanimation , Anesthésie Samu Urgences Réanimation, CHU Angers, France

27) Department of Haematology, PathWest Laboratory Medicine, University of Western Australia, Royal Perth Hospital, Perth, Western Australia

28) Hong Kong Red Cross Blood Transfusion Service, Hong Kong SAR, China

29) Department of Obstetrics and Gynecology, Soonchunhyang University Hospital, Seoul, Korea

30) Division Clinical Haematology, Department of Medicine, University of Cape Town, Cape Town, South Africa

31) Clinic of Anesthesiology and Intensive Care Medicine, Johannes Kepler University Linz, Austria

32) Vifor Pharma, Glattbrugg, Switzerland

33) Department of Surgical Sciences, Biochemistry and Immunology, School of Medicine, University of Málaga, Málaga, Spain

34) Patient Blood Management, Englewood Health, Englewood, NJ, USA

35) Department of Anesthesiology and Intensive Care, IRCCS Policlinico S. Donato, S. Donato Mil.se, Milan, Italy

36) Jerry M. Wallace School of Osteopathic Medicine, Campbell University, Buies Creek NC, USA

37) Institute of Anesthesiology, University of Zurich and University Hospital Zurich, Zurich, Switzerland

38) Department of Anesthesiology, University of Florida College of Medicine, Gainesville, FL, USA

39) South African National Blood Service, Johannesburg, South Africa

40) Medical School, The University of Western Australia, Perth, Australia; Data and Digital Innovation, East Metropolitan Health Service, Perth, Australia

41) Center for Health Law and Management, University of Bern, Bern, Switzerland

42) Institute of Anesthesiology, University Hospital and University Zurich, Zurich, Switzerland; Medical School, The University of Western Australia, Crawley, Australia; School of Health Sciences and Graduate Studies, Curtin University, Perth, Australia

Corresponding Author: Aryeh Shander, MD, Department of Anesthesiology, Critical Care and Hyperbaric Medicine, Englewood Health, 350 Engle Street, Englewood, NJ 07631, USA. Tel: 201 894 3238, Fax: 201 894 0585, Email: aryeh.shander@ehmchealth.org

Funding Received for the Work: None

Conflict of Interests: AS has been a consultant for Masimo corp, Vifor, Octapharma, CSL Bhering, HBO2 therapeutics, Daiichi, Grifols and Baxter and a speaker for Merck.

SMG is PBM executive section editor for A&A, has served as scientific data safety & monitoring chair for an Octapharma trial, has been a sponsored speaker for Masimo and was scientific advisory consultant for Haemonetics.

MA has received consulting fees from Vifor Pharma.

EB has received honoraria for lectures and/or travel support from Vifor Pharma, OM-Pharma, Takeda, Sysmex and Zambon.

AAPC has received honoraria from LFB, Octapharma, IL Werfen, Cheetah Medical, Baxter, Vifor and Takeda.

JC has received research support from Canadian Blood Services, Canadian Institute for Health Research, CSL Behring and Octpharma.

MMC has received honoraria from Cerus and Octapharma for consulting.

WBD has been an employee of the Australian Red Cross Lifeblood.

JE has received honoraria for lecturing from Vifor.

SF has received travel and meeting support, National Blood Authority (Australia).

SMF is on scientific advisory boards for Haemonetics, Medtronic, and Baxter.

BF has received financial support to give lectures, undertake research, attend scientific advisory boards, and undertake consultancies for the New South Wales Department of Health, South Australia Department of Health, Australian Red Cross Blood Service, Australian National Blood Authority, Vifor Pharma Ltd., Switzerland, Pharmacosmos A/S Denmark, Pfizer Australia and CSL Behring Australia,

IG received consulting fees from Accumen, Inc, Phoenix Arizona, in his role as Senior Medical Advisor

TH has been a consultant for Octapharma,

DJK is on the Scientific Advisory Board with Terumo Medical Corporation, Consultant with Instrumentation Laboratory, UpToDate, Consultant at the NIH and received Grant Funding from NIH.

SL is consultant for Vifor Pharma, has been a sponsored speaker for Masimo, Vifor, Pfizer and was scientific advisory consultant for iSep.

SL is the investigator coordinator of the HiFIT study, for which Pharamcosmos gives iron for free.

VLL received honoraria and/or travel support and/or grant funding from the following: Acino, Austell, Novartis Oncology, Pharmacosmos, Takeda, Vifor and I serve as a non-executive director on the Board of the Western Cape Blood Service.

AM is an employee of Vifor Pharma.

MM received honoraria for consultancy and/or lectures from Pharmacosmos, Pharmanutra, Vifor Pharma, Zambon and Celgene.

DRS has received honoraria and travel support for consulting or lecturing from Danube University of Krems, Austria, European Society of Anesthesiology, Brussels, BE, Bayer Pharma AG, Berlin, Germany, B. Braun Melsungen AG, Melsungen, Germany, CSL Behring GmbH, Hattersheim am Main, Germany and Berne, Switzerland, Daiichi Sankyo AG, Thalwil, Switzerland, Haemonetics, Braintree, MA, USA, Instrumentation Laboratory (Werfen), Bedford, MA, USA, LFB Biomédicaments, Courtaboeuf Cedex, France, Octapharma AG, Lachen, Switzerland, PAION Deutschland GmbH, Aachen, Germany, Pharmacosmos A/S, Holbaek, Denmark, Pierre Fabre Pharma, Alschwil, Switzerland, Vifor Pharma, Munich, Germany, Vienna, Austria and Villars-sur-Glâne, Switzerland, Vifor (International) AG, St. Gallen, Switzerland, Zuellig Pharma Holdings, Singapore, Singapore.

DRS's academic department is receiving grant support from the Swiss National Science Foundation, Berne, Switzerland, the Swiss Society of Anesthesiology and Reanimation (SGAR), Berne, Switzerland, the Swiss Foundation for Anesthesia Research, Zurich, Switzerland, Vifor SA, Villars-sur-Glâne, Switzerland. DRS is co-chair of the ABC-Trauma Faculty, sponsored by unrestricted educational grants from Novo Nordisk Health Care AG, Zurich, Switzerland, CSL Behring GmbH, Marburg, Germany, LFB Biomédicaments, Courtaboeuf Cedex, France and Octapharma AG, Lachen, Switzerland.

BS was a paid consultant to Hemosonics.

AH has received honoraria and/or travel support from IL Werfen, Celgene, G1 Therapeutics, Vifor and Takeda.

MJ has been a consultant for SABM and Gauss Surgical.

MAW, DF, TF, HG, NRG, JH, JPI, HWJ, YWK, JK, MFL, CKL, JJL, JM, SO, MP, NS, JT, KT and CZ declare no relevant conflict of interests.

Word Count for Body of Text: 2547

Word Count for Abstract: 268

Abbreviated Title: The role of PBM in Pandemics

Author Contributions: Aryeh Shander: This author initiated the call for action, developed the first draft, developed the ABC Toolbox for PBM, and critically revised the draft and approved the final version to be published.

Susan Marie Goobie: This author developed the first draft, developed the ABC Toolbox for PBM, and critically revised the draft and approved the final version to be published.

Matthew A Warner: This author developed the first draft and critically revised the draft and approved the final version to be published.

Matti Aapro: This author critically revised the draft and approved the final version to be published.

Elvira Bisbe: This author critically revised the draft and approved the final version to be published.

Angel A Perez-Calatayud: This author helped in identifying additional references and critically revised the draft and approved the final version to be published.

Jeannie Callum: This author critically revised the draft and approved the final version to be published.

Melissa M Cushing: This author critically revised the draft and approved the final version to be published.

Wayne B Dyer: This author critically revised the draft and approved the final version to be published.

Jochen Erhard: This author critically revised the draft and approved the final version to be published.

David Faraoni: This author critically revised the draft and approved the final version to be published.

Shannon Farmer: This author developed the ABC Toolbox for PBM and critically revised the draft and approved the final version to be published.

Tatyana Fedorova: This author critically revised the draft and approved the final version to be published.

Steven M Frank: This author critically revised the draft and approved the final version to be published.

Bernd Froessler: This author critically revised the draft and approved the final version to be published.

Hans Gombotz: This author critically revised the draft and approved the final version to be published.

Irwin Gross: This author helped in identifying additional references and critically revised the draft and approved the final version to be published.

Nicole R Guinn: This author critically revised the draft and approved the final version to be published.

Thorsten Haas: This author critically revised the draft and approved the final version to be published.

Jeffrey Hamdorf: This author developed the ABC Toolbox for PBM and critically revised the draft and approved the final version to be published.

James P Isbister: This author critically revised the draft and approved the final version to be published.

Mazyar Javidroozi: This author critically revised the draft and approved the final version to be published.

Hongwen Ji: This author critically revised the draft and approved the final version to be published.

Young-Woo Kim: This author critically revised the draft and approved the final version to be published.

Daryl J Kor: This author critically revised the draft and approved the final version to be published.

Johann Kurz: This author critically revised the draft and approved the final version to be published.

Sigismond Lasocki: This author critically revised the draft and approved the final version to be published.

Michael F Leahy: This author critically revised the draft and approved the final version to be published.

Cheuk-Kwong Lee: This author critically revised the draft and approved the final version to be published.

Jeong Jae Lee: This author critically revised the draft and approved the final version to be published.

Vernon Louw: This author critically revised the draft and approved the final version to be published.

Jens Meier: This author critically revised the draft and approved the final version to be published.

Anna Mezzacasa: This author critically revised the draft and approved the final version to be published.

Manuel Munoz: This author critically revised the draft and approved the final version to be published.

Sherri Ozawa: This author developed the ABC Toolbox for PBM and critically revised the draft and approved the final version to be published.

Marco Pavesi: This author critically revised the draft and approved the final version to be published.

Nina Shander: This author critically revised the draft and approved the final version to be published.

Donat R Spahn: This author helped in identifying additional references and critically revised the draft and approved the final version to be published.

Bruce D Spiess: This author critically revised the draft and approved the final version to be published.

Jackie Thomson: This author critically revised the draft and approved the final version to be published.

Kevin Trentino: This author critically revised the draft and approved the final version to be published.

Christoph Zenger: This author critically revised the draft and approved the final version to be published.

Axel Hofmann: This author initiated the call for action, developed the first draft, developed the ABC Toolbox for PBM and critically revised the draft and approved the final version to be published.

Abstract

The World Health Organization (WHO) has declared Coronavirus Disease 2019 (COVID-19), the disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a pandemic. Global health care now faces unprecedented challenges with widespread and rapid human-to-human transmission of SARS-CoV-2 and high morbidity and mortality with COVID-19 worldwide. Across the world, the medical care is hampered by a critical shortage of not only hand sanitizers, personal protective equipment, ventilators and hospital beds, but also impediments to the blood supply. Blood donation centers in many areas around the globe have mostly closed. Donors, practicing social distancing, some either with illness or undergoing self-quarantine, are quickly diminishing. Drastic public health initiatives have focused on containment and "flattening the curve" while invaluable resources are being depleted. In some countries, the point is reached at which demand for such resources, including donor blood outstrips supply. Questions as to the safety of blood persist. Although it does not appear very likely that the virus can be transmitted through allogeneic blood transfusion, this still remains to be fully determined. As options dwindle, we must enact regional and national shortage plans worldwide, and more vitally disseminate the knowledge of and immediately implement Patient Blood Management (PBM). PBM is an evidence-based bundle of care to optimize medical and surgical patient outcomes by clinically managing and preserving a patient's own blood. This multinational and diverse group of authors issue this "Call to Action" underscoring "The Essential Role of Patient Blood Management in the Management of Pandemics" and urging all stakeholders and providers to implement the practical and common-sense principles of PBM and its multi-professional and multimodality approaches.

Glossary of Terms:

ANH, acute normovolemic hemodilution

COVID-19, Coronavirus Disease 2019

DOAC, direct oral anticoagulants

ECDC, European Centre for Disease Prevention and Control

ESA, erythropoiesis-stimulating agent

FiO2, fraction of inspired oxygen

H1N1, influenza A virus subtype H1N1

NAT, nucleic acid testing

NSAID, nonsteroidal anti-inflammatory drug

PBM, patient blood management

PCC, prothrombin complex concentrate

PPI, proton-pump inhibitor

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

TACO, transfusion-associated circulatory overload

TRALI, transfusion-related acute lung injury

WHO, World Health Organization

Background

Given the recent emergence of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the ensuing worldwide, widespread human-to-human transmission of the related Coronavirus Disease 2019 (COVID-19), the World Health Organization (WHO) has declared a pandemic status for this virus and the virus-related disease. As one of the corollaries, public health authorities and blood services are concerned with decreasing blood donations, ultimately resulting in blood shortages that will unquestionably lead to difficult and controversial transfusion rationing decisions by frontline health care providers. Considering that blood is a perishable commodity with a very short expiration time, as with past pandemics, blood services are being challenged to maintain their inventory during the current COVID-19 pandemics. On the other hand, analyses after past natural and man-made disasters have demonstrated either no change or a reduction in the demand for blood and its use.[1,2]

Blood Supply Challenges During Pandemics

The influenza A virus subtype H1N1 (H1N1) pandemic had a significant impact on the blood supply due to donors' fear of exposure to the virus at a hospital or a free-standing donor faculity.[3,4] Similarly, the COVID-19 pandemic has already led to significantly reduced blood supplies due to the cancellation of numerous community-based and mobile blood drives, as well as a marked reduction in donors arriving for scheduled appointments. For instance, as a result of the current pandemic and restrictions on congregating through social distancing, to date in the U.S., nearly 4000 American Red Cross blood drives have been canceled across the country. Hospital-based collections have been cancelled due to institutional concerns regarding donors spreading COVID-19 to hospitalized patients or vice versa. These cancellations have resulted in some 130,000 fewer blood donations in only a few weeks. More than 80% of the blood the American Red Cross collects comes from drives

held at non-permanent collection locations. According to the Chief Executive Officer of New York Blood Center, the main blood supplier for New York City, around 75% of their incoming blood supply was interrupted during the week of March 16, 2020, when schools, businesses and religious institutions closed due to the coronavirus outbreak.[5]

Moreover, the number of eligible donors in the course of a pandemic will inevitably decrease due to an increasing number of individuals being infected or in self-quarantine after exposure to infected persons or persons under investigation. In addition, blood collection facilities have put additional screening criteria in place, declining donors with history of travel from infection "hot spots" in the preceding 14 days, at a time when a large proportion of the population had travelled for school spring breaks. Finally, older persons, who often represent the most reliable donor pool, are also apparently among the most vulnerable to the COVID-19 pandemic.

The default response to reduced blood supplies and the limited capacity of health care facilities is the suspension of elective surgical procedures regardless of the lack of uniform definitions for "elective."[6] Yet, blood utilization for urgent and emergent interventions that can actually represent a greater demand on the blood supply is likely to remain unchanged. The same will likely be true for chronically transfusion-dependent patients, including those with malignancies, hematological conditions (e.g., sickle cell, thalassemia, myelodysplastic syndrome) and chemotherapy-induced anemia. In some cases, cancellation of elective surgeries may permit disease progression resulting in more complex and urgent situations, as the pandemic further progresses.

Calls from blood centers for more donors do not sufficiently alleviate this problem. In the context of pandemics, the pressure on blood collection facilities and hospital transfusion medicine services and their staff is also increased as more and more staff members are required to self-isolate, self-quarantine or become ill. In addition, the effort to continue

standard blood donor recruitment will be diverted in part by the growing initiative to manufacture convalescent plasma from patients who have recovered from COVID-19. While this treatment option remains under investigation on a limited basis and is not currently a major source of demand for blood donations, the rapidly evolving nature of the pandemic might quickly change the landscape, creating a substantial new demand.

It should also be noted that supply chains are often affected by travel restrictions, factory closings, and decreased manufacturing output, which may in turn affect the ability of blood services to maintain their testing and production facilities in times of increasing need.

Another remote but significant issue is possible virus transmission via donated blood. At some stage of the pandemic, we expect that a considerable percentage of the population will be unknowingly infected by SARS-CoV-2, including the young blood donor population in which asymptomatic cases will be common. In the absence of nucleic acid testing (NAT) for blood donor screening for SARS-CoV-2, we cannot exclude, albeit theoretical at this time, the possible transmission via a blood transfusion, if some of the donated blood may be contaminated.[7] Thus, we are facing significant unknowns, and only future studies will elucidate the true risks of transfusion-transmitted SARS-CoV-2 if any.[8]

The Essential Role of Patient Blood Management

For all of the above reasons, the medical community must adopt other solutions to continue and/or resume care of our patient population. Thus, the immediate and global implementation of Patient Blood Management (PBM) should be mandated.[9,10] PBM is defined as an evidence-based bundle of care to optimize medical and surgical patient outcomes by clinically managing and preserving a patient's own blood (www.ifpbm.org) or alternatively, as the timely application of evidence-based medical concepts designed to maintain hemoglobin concentration, optimize hemostasis, and minimize blood loss, in an effort to improve patient outcomes (www.sabm.org).

The National Blood Authority (Australia) evidence-based PBM Guidelines are an exhaustive systematic review of the literature with an attendant rigorous methodology for developing recommendations, practice points, and expert opinion points. The six modules contain 52 Recommendations, 142 Practice Points and 56 Expert Opinion Points. The PBM Toolbox (Tables 1 and 2) summarizes the practical concepts of PBM.[11-65]

Numerous large observational studies,[33,66,67] several randomized controlled trials[30,68-70] and meta-analyses[31,71] have demonstrated significantly improved patient outcomes with PBM, while substantially reducing blood utilization. The concept of PBM proactively focuses on patient needs as well as the conditions that usually lead to transfusions, namely, blood loss, coagulopathies, platelet dysfunction and anemia. PBM shifts the focus from reactive transfusion of patients with allogeneic blood components, to preventive measures by optimally managing the patient's own blood.

The PBM concept was endorsed in 2010 by the World Health Assembly through resolution WHA63.12. In 2017 it was recommended as standard of care by the European Commission. In the recent WHO Action Framework to advance universal access to safe, effective and quality assured blood components in 2020-2023, the effective implementation of PBM is listed as one of six goals.[72] Despite these strong recommendations and the available evidence demonstrating that the PBM model is not just an option but rather a necessity, practice change still lags very far behind. Furthermore, while expert consensus demonstrates that the PBM model improves clinical outcomes, increases patient safety and reduces costs, hospitals with organized PBM programs are few and far between.

Call to Action

In the face of the current crisis, the European Centre for Disease Prevention and Control (ECDC) in its rapid risk assessment of March 12, 2020 on COVID-19 states that the "Implementation of Patient Blood Management (PBM) … is strongly advisable."

Furthermore, the interim guidance on March 20, 2020 from the WHO on maintaining a safe and adequate blood supply during the COVID-19 pandemic recommends, "Good patient blood management" to safeguard blood stocks.[73] In the current pandemic setting, both the severe limitation of available healthcare resources and the growing shortage of donor blood clearly support that the rapid implementation of PBM is the optimal way forward. Beyond beneficial effects on blood utilization, PBM-associated improvements in clinical outcomes, specifically, a reduction in hospital-acquired infections and reduced lengths of stay, may further decrease the burden on an overwhelmed healthcare system.

Therefore, healthcare leaders and clinicians are urged and called on to immediately champion change and improve their institutional infrastructure and processes to ensure the following:

1. Identify, evaluate and treat iron deficiency and anemia in both medical and surgical patients with appropriate pharmacological agents.[24,74,75]

In 2015, a total of 2.36 billion people or 32% of the world population were affected by anemia, representing the most prevalent of all impairments globally. In more than 60% of all cases, iron deficiency was the cause of anemia.[76] However, the prevalence of anemia in hospitalized patients is significantly higher than in the general population and can reach up to 75% in specific surgical populations.[77] Anemia is associated with increased blood utilization, worse patient outcomes and increased morbidity and mortality in surgical and medical patients of all ages.[78,79]

Prevention, early diagnosis, and prompt treatment directed by the etiology of anemia can decrease blood utilization and improve patient outcomes. Iron deficiency, with and without anemia, is common and is associated with increased mortality in cardiac surgery[80] and may be treated with oral or intravenous iron supplementation. Oral therapy is often poorly tolerated, has a slower onset of action than intravenous iron, and is insufficient to

correct iron deficiency in the presence of ongoing bleeding. Intravenous iron therapy is preferred for those with intolerance to oral therapy, severe anemia (i.e. hemoglobin <10 g/dL) or planned surgical procedures or obstetrical delivery within six weeks. There are many formulations that allow for rapid, safe and complete correction of iron deficiency. Women and adolescent girls presenting for obstetrical care or with menorrhagia to emergency medicine departments with severe iron deficiency must be offered intravenous iron to mitigate the risk of a preventable transfusion.[81,82] Anemia related to other nutritional deficiencies, such as folate and vitamin B12 may, in many cases, be corrected with oral therapy, with both folate and vitamin B12 typically dosed at 1 mg daily.

Erythropoiesis-stimulating agents (ESAs) are exogenous forms of erythropoietin, including epoetin alfa, the longer-acting darbepoetin alfa, and other emerging ESAs, which may be utilized to stimulate erythropoiesis. While ESAs are often used in the long-term management of anemia in patients with chronic kidney disease and chemotherapy-induced bone marrow suppression, there has been increasing expansion to short-term use in those with preoperative anemia, particularly when anemia is deemed secondary to anemia of inflammation.[37] In preoperative patients and in the critically ill, ESA utilization with either 100,000 units weekly in the ICU or 600/kg in the preoperative period results in higher hemoglobin concentrations and reduced transfusion utilization.[70]

2. *Identify and rapidly address coagulation/hemostatic issues perioperatively.*[23]

Coagulopathy, when not promptly recognized and corrected, can perpetuate a cycle of bleeding, blood utilization, and patient morbidity. There are several evidence-based strategies available for appropriate management of coagulopathy. Point-of-care viscoelastic testing, including thromboelastography and rotational thromboelastometry, facilitates near real-time identification of coagulation abnormalities, thereby allowing rapid and targeted correction of

the impaired pathway, rather than relying on unguided administration of plasma and platelets.[83,84]

Transfusion therapies can often be avoided altogether by the utilization of clotting factors such as prothrombin complex concentrates or fibrinogen concentrate. In addition to transfusion-sparing effects, clotting factors also decrease the risk for transfusion-related complications, such as transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO), the leading causes of transfusion-related morbidity and mortality.[85] Antifibrinolytic agents, including tranexamic acid and epsilon aminocaproic acid, are widely available, inexpensive, highly effective and safe pharmacologic agents that may be utilized to stabilize clot formation and prevent hyperfibrinolysis. The use of these agents has consistently been associated with bleeding reduction, transfusion reduction and improved outcomes across numerous surgical procedures and in trauma settings.[43,86]

3. *Use all effective blood conservation methods in both medical and surgical patients.*[87]

There are numerous modalities available for perioperative blood conservation. These include avoiding hemodilution, restrictive transfusion strategies for all types of allogeneic blood components,[55-58,88] optimizing physiologic response to anemia, early treatment of coagulopathy, and the use of topical hemostatic agents.

Cell salvage, which involves the collection of a patient's own blood loss, filtering and washing to ensure the removal of impurities, and direct return of the autologous component to the patient, is associated with reductions in allogeneic blood component utilization. Therefore, it is recommended for all procedures with moderate-to-large volume blood loss.[34,89]

Acute normovolemic hemodilution (ANH) is a process by which a controlled volume of a patient's own blood is removed prior to the surgical insult followed by replacement with crystalloids or colloids.[90] In adults, this results in less red blood cell loss during the surgical

procedure and allows for the reinfusion of autologous blood, rich in red blood cells, platelets, and clotting factors, when it is needed intraoperatively or postoperatively.[91] ANH provides autologous fresh whole blood or can be sequestered to deliver red cells, plasma or platelets as needed, but its use is more likely to be beneficial in procedures with significant blood loss. ANH should thus be considered on a case by case basis.

For both medical and surgical patients, it is also essential to limit iatrogenic blood loss. Most often this occurs through diagnostic phlebotomy. Methods to reduce iatrogenic blood loss include the minimization of unnecessary blood sampling, the use of pediatric small vacuum blood draws, which allow for testing on hospital automated chemistry lines, and the employment of closed-loop sampling devices.[37]

4. ***Carefully monitor patients' condition after surgery and rapidly intervene by either interventional radiology and/or endoscopy for unexpected bleeding depending on the source.***

Bleeding postoperatively and post-obstetrical delivery is common and is associated with increased resource utilization and worse clinical outcomes. Therefore, it is essential that all patients receive serial evaluation for bleeding, including assessments of drain output, frequent monitoring for hemodynamic status, and physical examination. In patients with suspected bleeding or coagulopathy, point-of-care viscoelastic testing and hemoglobin assessments may be used for the rapid identification of bleeding and coagulation abnormalities, as well as the rapid employment of surgical and interventional radiology intervention to immediately achieve source control.

5. ***Thoroughly inform and educate medical professionals, patients and their caregivers on the importance of PBM. Involve patients in treatment and management decisions and obtain formal consent.***

It is important to involve these key stakeholders in the decision-making process and letting them know that their well-being and the health of their loved ones is at the center of this comprehensive effort. Patients who are chronically transfused need prompt and frequent messaging to reassure them that all efforts are being deployed to maintain their access to transfusion. Difficult decisions will need to be made for patients requiring massive transfusion for traumatic injury, gastrointestinal bleeding, and cardiovascular surgery—all with a very poor chance of short-term and long-term survival. Transfusing multiple units of blood components to a single patient is not only associated with high morbidity and mortality but such massive transfusions could also compromise the transfusion support for many other patients in need.[92]

Conclusion

Faced with the substantial challenges during the COVID-19 pandemic that has left no one worldwide safe or unaffected, medical contributions—large or small—are urgently needed to provide the optimal and most compassionate care while using every modality to conserve resources. Appropriate resource conservation will allow for better allocation to those patients in absolute need. The authors of this "Call for Action" document represent diverse backgrounds and specialties, yet they come together with a cohesive message, underscoring "The Essential Role of Patient Blood Management in the Management of Pandemics" and urging all to implement the practical and common-sense principles of PBM and its multi-professional and multimodality approaches.

Contributors:

This manuscript is prepared and presented on behalf of the International Foundation of Patient Blood Management (IFPBM) and Society for the Advancement of Blood Management (SABM) Work Group. All members of the work groups are also authors of the manuscript and they include Aryeh Shander, Susan Marie Goobie, Matti Aapro, Elvira Bisbe, Melissa M Cushing, Wayne B Dyer, Jochen Erhard, Shannon Farmer, Bernd Froessler, Hans Gombotz, Irwin Gross, Thorsten Haas, Jeffrey Hamdorf, James P Isbister, Hongwn Ji, Young-Woo Kim, Sigismond Lasocki, Michael F Leahy, Jeong Jae Lee, Jens Meier, Sherri Ozawa, Marco Pavesi, Donat R Spahn, Bruce D Spiess, Kevin Trentino, Christoph Zener and Axel Hofmann for IFPBM and Aryeh Shander, Susan Marie Goobie, Melissa M Cushing, Steven M Frank, Irwin Gross, Nicole R Guinn, Daryl J Kor, Sherri Ozawa, Bruce D Spiess and Axel Hofmann for SABM.

References

1. Schmidt PJ. Blood and disaster--supply and demand. The New England journal of medicine 2002;346:617-20.

2. Zaheer HA, Waheed U. Blood transfusion service in disasters. Transfus Apher Sci 2016;55:186-90.

3. Landro L. New Flu Victim: Blood Supply. The Wall Street Journal November 10, 2009.

4. Maintaining a Safe and Adequate Blood Supply during Pandemic Influenza - Guidelines for Blood Transfusion Services. World Health Organization, 2011. at https://www.who.int/bloodsafety/publications/WHO_Guidelines_on_Pandemic_Influenza_and_Blood_Supply.pdf.)

5. New York Blood Center Expand Capacity at Donors Centers; Urges Healthy Donors to Schedule Appointments to Maintain Blood Supply at this Critical Time. New York Blood Center. (Accessed March 25, 2020, at https://nybloodcenter.org/news/articles/new-york-blood-center-expands-capacity-donors-centers-urges-healthy-donors-schedule-appointments-maintain-blood-supply-critical-time/.)

6. McCauley D. Morrison launches COVID-19 Coordination Commission, cancels non-urgent surgery. The Sydney Morning Herald March 25, 2020.

7. Chang L, Yan Y, Wang L. Coronavirus Disease 2019: Coronaviruses and Blood Safety. Transfus Med Rev 2020.

8. Statement on Coronavirus and Blood Donation. AABB. (Accessed March 23, 2020, at www.aabb.org/advocacy/regulatorygovernment/Pages/Statement-on-Coronavirus-and-Blood-Donation.aspx.)

9. Hofmann A, Farmer S, Shander A. Five drivers shifting the paradigm from product-focused transfusion practice to patient blood management. The Oncologist 2011;16 Suppl 3:3-11.

10. Spahn DR, Munoz M, Klein AA, Levy JH, Zacharowski K. Patient Blood Management: Effectiveness and Future Potential. Anesthesiology 2020.

11. Patient Blood Management Guidelines: Module 1 - Critical Bleeding / Massive Transfusion. National Blood Authority, 2011. (Accessed 15 September 2018, at http://www.blood.gov.au/pbm-module-1.)

12. Patient Blood Management Guidelines: Module 2 - Perioperative. National Blood Authority, 2012. (Accessed 15 September 2018, at http://www.blood.gov.au/pbm-module-2.)

13. Patient Blood Management Guidelines: Module 3 - Medical. National Blood Authority, 2012. (Accessed 15 September 2018, at http://www.blood.gov.au/pbm-module-3.)

14. Patient Blood Management Guidelines: Module 4 - Critical Care. National Blood Authority, 2012. (Accessed 15 September 2018, at http://www.blood.gov.au/pbm-module-4.)

15. Patient Blood Management Guidelines: Module 5 - Obstetrics. National Blood Authority, 2015. (Accessed 15 September 2018,

16. Patient Blood Management Guidelines: Module 6 - Neonatal and Paediatrics. National Blood Authority, 2017. (Accessed 15 September 2018, 2018, at https://www.blood.gov.au/patient-blood-management-pbm.)

17. Munoz M, Pena-Rosas JP, Robinson S, et al. Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. Transfus Med 2017.

18. Faraoni D, Meier J, New HV, Van der Linden PJ, Hunt BJ. Patient Blood Management for Neonates and Children Undergoing Cardiac Surgery: 2019 NATA Guidelines. J Cardiothorac Vasc Anesth 2019;33:3249-63.

19. Goobie SM, Gallagher T, Gross I, Shander A. Society for the advancement of blood management administrative and clinical standards for patient blood management programs. 4th edition (pediatric version). Paediatr Anaesth 2019;29:231-6.

20. SABM Administrative and Clinical Standards for Patient Blood Management Programs, 4th edition. Society for the Advancement of Blood Management, 2017. (Accessed 15 September 2018, at https://www.sabm.org/publications/.)

21. Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic S, the European Association of Cardiothoracic A, Boer C, et al. 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery. J Cardiothorac Vasc Anesth 2017.

22. Spahn DR, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care 2019;23:98.

23. Kozek-Langenecker SA, Ahmed AB, Afshari A, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: First update 2016. Eur J Anaesthesiol 2017;34:332-95.

24. Aapro M, Beguin Y, Bokemeyer C, et al. Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. Ann Oncol 2018.

25. Pavord S, Myers B, Robinson S, et al. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol 2012;156:588-600.

26. Kotter JP. Leading change. Boston, Mass.: Harvard Business School Press; 1996.

27. Kotter JP, Cohen D. The heart of change. Boston, Mass.: Harvard Business School Press; 2002.

28. Gombotz H, Hofmann A, Nørgaard A, Kastner P. Supporting Patient Blood Management (PBM) in the EU - A Practical Implementation Guide for Hospitals. Luxembourg: European Commission - Directorate-General for Health and Food Safety 2017.

29. Hofmann A, Nørgaard A, Kurz J, et al. Building national programmes of Patient Blood Management (PBM) in the EU - A Guide for Health Authorities. Luxembourg: European Commission - Directorate-General for Health and Food Safety 2017.

30. Weber CF, Gorlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. Anesthesiology 2012;117:531-47.

31. Deppe AC, Weber C, Zimmermann J, et al. Point-of-care thromboelastography/thromboelastometry-based coagulation management in cardiac surgery: a meta-analysis of 8332 patients. J Surg Res 2016;203:424-33.

32. Karkouti K, Callum J, Wijeysundera DN, et al. Point-of-Care Hemostatic Testing in Cardiac Surgery: A Stepped-Wedge Clustered Randomized Controlled Trial. Circulation 2016;134:1152-62.

33. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. Transfusion 2017;57:1347-58.

34. Klein AA, Bailey CR, Charlton AJ, et al. Association of Anaesthetists guidelines: cell salvage for peri-operative blood conservation 2018. Anaesthesia 2018;73:1141-50.

35. Zhou X, Zhang C, Wang Y, Yu L, Yan M. Preoperative Acute Normovolemic Hemodilution for Minimizing Allogeneic Blood Transfusion: A Meta-Analysis. Anesth Analg 2015;121:1443-55.

36. Kaserer A, Kiavialaitis GE, Braun J, et al. Impact of rivaroxaban plasma concentration on perioperative red blood cell loss. Transfusion 2020;60:197-205.

37. Warner MA, Shore-Lesserson L, Shander A, Patel SY, Perelman SI, Guinn NR. Perioperative Anemia: Prevention, Diagnosis, and Management Throughout the Spectrum of Perioperative Care. Anesth Analg 2020.

38. von Haehling S, Ebner N, Evertz R, Ponikowski P, Anker SD. Iron Deficiency in Heart Failure: An Overview. JACC Heart failure 2019;7:36-46.

39. Weiss G, Goodnough LT. Anemia of chronic disease. The New England journal of medicine 2005;352:1011-23.

40. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program 2015;2015:8-13.

41. Devalia V, Hamilton MS, Molloy AM, British Committee for Standards in H. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. Br J Haematol 2014;166:496-513.

42. Green R. Vitamin B12 deficiency from the perspective of a practicing hematologist. Blood 2017;129:2603-11.

43. Goobie SM, Faraoni D. Tranexamic acid and perioperative bleeding in children: what do we still need to know? Curr Opin Anaesthesiol 2019;32:343-52.

44. Lier H, Maegele M, Shander A. Tranexamic Acid for Acute Hemorrhage: A Narrative Review of Landmark Studies and a Critical Reappraisal of Its Use Over the Last Decade. Anesth Analg 2019;129:1574-84.

45. Pavenski K, Ward SE, Hare GMT, et al. A rationale for universal tranexamic acid in major joint arthroplasty: overall efficacy and impact of risk factors for transfusion. Transfusion 2019;59:207-16.

46. Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. Br J Surg 2013;100:1271-9.

47. Lin DM, Murphy LS, Tran MH. Use of prothrombin complex concentrates and fibrinogen concentrates in the perioperative setting: a systematic review. Transfus Med Rev 2013;27:91-104.

48. Beris P, Munoz M, Garcia-Erce JA, Thomas D, Maniatis A, Van der Linden P. Perioperative anaemia management: consensus statement on the role of intravenous iron. BJA 2008;100:599-04.

49. Shander A, Javidroozi M, Ashton ME. Drug-induced anemia and other red cell disorders: a guide in the age of polypharmacy. Curr Clin Pharmacol 2011;6:295-303.

50. Mikhail A, Brown C, Williams JA, et al. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. BMC Nephrol 2017;18:345.

51. Macdougall IC, Canaud B, de Francisco AL, et al. Beyond the cardiorenal anaemia syndrome: recognizing the role of iron deficiency. Eur J Heart Fail 2012;14:882-6.

52. Schmied H, Kurz A, Sessler DI, Kozek S, Reiter A. Mild hypothermia increases blood loss and transfusion requirements during total hip arthroplasty. Lancet 1996;347:289-92.

53. Whitehead NS, Williams LO, Meleth S, et al. Interventions to prevent iatrogenic anemia: a Laboratory Medicine Best Practices systematic review. Crit Care 2019;23:278.

54. Koch CG, Reineks EZ, Tang AS, et al. Contemporary bloodletting in cardiac surgical care. Ann Thorac Surg 2015;99:779-84.

55. Valentine SL, Bembea MM, Muszynski JA, et al. Consensus Recommendations for RBC Transfusion Practice in Critically Ill Children From the Pediatric Critical Care Transfusion and Anemia Expertise Initiative. Pediatr Crit Care Med 2018;19:884-98.

56. Mazer CD, Whitlock RP, Fergusson DA, et al. Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery. N Engl J Med 2017.

57. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013;368:11-21.

58. Holst LB, Haase N, Wetterslev J, et al. Lower versus Higher Hemoglobin Threshold for Transfusion in Septic Shock. N Engl J Med 2014.

59. Ma M, Eckert K, Ralley F, Chin-Yee I. A retrospective study evaluating single-unit red blood cell transfusions in reducing allogeneic blood exposure. Transfusion medicine 2005;15:307-12.

60. Naylor JM, Adie S, Fransen M, Dietsch S, Harris I. Endorsing single-unit transfusion combined with a restrictive haemoglobin transfusion threshold after knee arthroplasty. Quality & safety in health care 2010;19:239-43.

61. Berger MD, Gerber B, Arn K, Senn O, Schanz U, Stussi G. Significant reduction of red blood cell transfusion requirements by changing from a double-unit to a single-unit transfusion policy in patients receiving intensive chemotherapy or stem cell transplantation. Haematologica 2012;97:116-22.

62. Warwick R, Mediratta N, Chalmers J, et al. Is single-unit blood transfusion bad post-coronary artery bypass surgery? Interact Cardiovasc Thorac Surg 2013;16:765-71.

63. Mukhtar SA, Leahy MF, Koay K, et al. Effectiveness of a patient blood management data system in monitoring blood use in Western Australia. Anaesth Intensive Care 2013;41:207-15.

64. Trentino KM, Swain SG, Geelhoed GC, Daly FF, Leahy MF. Interactive patient blood management dashboards used in Western Australia. Transfusion 2016.

65. Sazama K. The ethics of blood management. Vox sanguinis 2007;92:95-102.

66. Keding V, Zacharowski K, Bechstein WO, Meybohm P, Schnitzbauer AA. Patient Blood Management improves outcome in oncologic surgery. World J Surg Oncol 2018;16:159.

67. Gani F, Cerullo M, Ejaz A, et al. Implementation of a Blood Management Program at a Tertiary Care Hospital: Effect on Transfusion Practices and Clinical Outcomes Among Patients Undergoing Surgery. Ann Surg 2019;269:1073-9.

68. Froessler B, Palm P, Weber I, Hodyl NA, Singh R, Murphy EM. The Important Role for Intravenous Iron in Perioperative Patient Blood Management in Major Abdominal Surgery: A Randomized Controlled Trial. Ann Surg 2016;264:41-6.

69. Khalafallah AA, Yan C, Al-Badri R, et al. Intravenous ferric carboxymaltose versus standard care in the management of postoperative anaemia: a prospective, open-label, randomised controlled trial. The Lancet Haematology 2016;3:e415-25.

70. Spahn DR, Schoenrath F, Spahn GH, et al. Effect of ultra-short-term treatment of patients with iron deficiency or anaemia undergoing cardiac surgery: a prospective randomised trial. Lancet 2019.

71. Althoff FC, Neb H, Herrmann E, et al. Multimodal Patient Blood Management Program Based on a Three-pillar Strategy: A Systematic Review and Meta-analysis. Ann Surg 2018.

72. WHO Action framework to advance universal access to safe, effective and quality assured blood products 2020-2023. World Health Organization. at https://www.who.int/news-room/detail/19-02-2020-who-action-framework-to-advance-universal-access-to-safe-effective-and-quality-assured-blood-products-2020--2023.)

73. Maintaining a safe and adequate blood supply during the pandemic outbreak of coronavirus disease (COVID-19). World Health Organization. (Accessed March 24, 2020, at https://www.who.int/publications-detail/maintaining-a-safe-and-adequate-blood-supply-during-the-pandemic-outbreak-of-coronavirus-disease-(covid-19).)

74. Munoz M, Acheson AG, Auerbach M, et al. International consensus statement on the peri-operative management of anaemia and iron deficiency. Anaesthesia 2017;72:233-47.

75. Shander A, Goodnough LT. From Tolerating Anemia to Treating Anemia. Ann Intern Med 2019;170:125-6.

76. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388:1545-602.

77. Munoz M, Gomez-Ramirez S, Kozek-Langeneker S, et al. 'Fit to fly': overcoming barriers to preoperative haemoglobin optimization in surgical patients. Br J Anaesth 2015;115:15-24.

78. Goobie SM, Faraoni D, Zurakowski D, DiNardo JA. Association of Preoperative Anemia With Postoperative Mortality in Neonates. JAMA pediatrics 2016;170:855-62.

79. Fowler AJ, Ahmad T, Abbott TEF, et al. Association of preoperative anaemia with postoperative morbidity and mortality: an observational cohort study in low-, middle-, and high-income countries. Br J Anaesth 2018;121:1227-35.

80. Rossler J, Schoenrath F, Seifert B, et al. Iron deficiency is associated with higher mortality in patients undergoing cardiac surgery: a prospective study. Br J Anaesth 2019.

81. Khadadah F, Callum J, Shelton D, Lin Y. Improving quality of care for patients with iron deficiency anemia presenting to the emergency department. Transfusion 2018;58:1902-8.

82. Froessler B, Gajic T, Dekker G, Hodyl NA. Treatment of iron deficiency and iron deficiency anemia with intravenous ferric carboxymaltose in pregnancy. Arch Gynecol Obstet 2018;298:75-82.

83. Wikkelso A, Wetterslev J, Moller AM, Afshari A. Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) to monitor haemostatic treatment in bleeding patients: a systematic review with meta-analysis and trial sequential analysis. Anaesthesia 2017;72:519-31.

84. Dias JD, Sauaia A, Achneck HE, Hartmann J, Moore EE. Thromboelastography-guided therapy improves patient blood management and certain clinical outcomes in elective cardiac and liver surgery and emergency resuscitation: A systematic review and analysis. J Thromb Haemost 2019;17:984-94.

85. Tanaka KA, Mazzeffi M, Durila M. Role of prothrombin complex concentrate in perioperative coagulation therapy. J Intensive Care 2014;2:60.

86. Stein P, Kaserer A, Sprengel K, et al. Change of transfusion and treatment paradigm in major trauma patients. Anaesthesia 2017;72:1317-26.

87. Sadana D, Pratzer A, Scher LJ, et al. Promoting High-Value Practice by Reducing Unnecessary Transfusions With a Patient Blood Management Program. JAMA internal medicine 2018;178:116-22.

88. Steinbicker AU, Wittenmeier E, Goobie SM. Pediatric non-red cell blood product transfusion practices: what's the evidence to guide transfusion of the 'yellow' blood products? Curr Opin Anaesthesiol 2020;33:259-67.

89. Carless PA, Henry DA, Moxey AJ, O'Connell D, Brown T, Fergusson DA. Cell salvage for minimising perioperative allogeneic blood transfusion. Cochrane Database Syst Rev 2010:CD001888.

90. Kreimeier U, Messmer K. Hemodilution in clinical surgery: state of the art 1996. World J Surg 1996;20:1208-17.

91. Barile L, Fominskiy E, Di Tomasso N, et al. Acute Normovolemic Hemodilution Reduces Allogeneic Red Blood Cell Transfusion in Cardiac Surgery: A Systematic Review and Meta-analysis of Randomized Trials. Anesth Analg 2017;124:743-52.

92. Johnson DJ, Scott AV, Barodka VM, et al. Morbidity and Mortality after High-dose Transfusion. Anesthesiology 2016;124:387-95.

93. Shaylor R, Weiniger CF, Austin N, et al. National and International Guidelines for Patient Blood Management in Obstetrics: A Qualitative Review. Anesth Analg 2017;124:216-32.

TABLES