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

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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.

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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.

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TABLES

Table 1- The ABC Toolbox for Patient Blood Management (PBM) (From the IFPBM-SABM Workgroup)

Table 2- Patient Blood Management (PBM) related guidelines and recommendations by specialty and/or clinical settings.

Table 1- The ABC Toolbox for Patient Blood Management (PBM) (from the IFPBM-SABM Workgroup)

Tools	Anemia and iron deficiency	Blood loss and bleeding	Coagulopathy
1. Program implementation methodology	• Change culture across your institution[26-28] • Disseminate evidence-based PBM guidelines/recommendations and detect and discourage non-evidence practices[11-16,19,23,93] • Translate evidence-based guidelines/recommendations into clinical practice[28,29] • Identify practice areas that need improvement		
2. Diagnostic devices	• Point-of-care hemoglobin analyzers • Point-of-care testing for iron deficiency if available	• Point-of-care coagulation and platelet function testing and goal-directed treatment[30-32] • Rapid diagnostic tests for presence of DOACs if available[36]	• Point-of-care coagulation and platelet function testing and goal-directed treatment[30-32] • Rapid diagnostic tests for presence of direct oral anticoagulants (DOACs) if available[36]
3. Treatment devices		• Pre- and post-operative cell recovery (cell saver)[34] • Acute normovolemic hemodilution (ANH)[35]	
4. Pharmaceuticals	• Oral/Intravenous iron[37-40] • Folic acid[41] • Vitamin B12[41,42] • Erythropoiesis-stimulating agents[37,39,40]	• Antifibrinolytics (tranexamic acid, aminocaproic acid)[43-46] • Topical hemostatic agents • Local vasoconstrictive agents • WBC and platelet-stimulating agents where appropriate • Consider high FIO_2 (1.0) in patients with life-threatening anemia	• Fibrinogen concentrate[47] • Prothrombin complex concentrate (PCC)[47] • Other clotting factors • Vitamin K intravenously
	• Educate physicians on indications and dosage		
5. Vigilance with nutritional and pharmacological interactions	Identify and manage drug therapies and/or nutrition that • Can contribute to anemia and hematinic deficiencies (e.g., PPIs) • Can increase iron absorption e.g. ascorbic acid • Can impair absorption e.g. some vitamin and herbal supplements, tea, coffee or dairy products	Identify and manage drug therapies and/or nutrition that increase the bleeding risk e.g. • NSAIDs (including COX2 inhibitors), antidepressants, statins, antiarrhythmics • Vitamin and herbal supplements including vitamin E, vitamin K, garlic, ginger, ginkgo biloba, fish oil, chamomile, dandelion root, etc.	
6. General principles	Identify, evaluate and manage anemia and iron deficiency.[37,48] • Evaluate and manage underlying disorders causing anemia and iron deficiency • Be aware of drugs associated with red blood cell disorders[49] • Anemia management program for pre-hospital, hospital and post-discharge patients • Focus on patients with comorbidities (diabetes, chronic kidney disease, congestive heart failure)[50,51]	• Meticulous surgical hemostasis • Optimize surgical technique • Patient positioning • Efforts to stop bleeding immediately • Minimally invasive surgical techniques • Restrictive fluid administration and permissive hypotension until bleeding is controlled • Achieve euvolemia once bleeding controlled • Deliberate induced hypotension • Careful blood pressure and fluid management • Prevent hypothermia[52], hypoperfusion and acidosis • Maintain normal circulating volume (euvolemia) • Minimize iatrogenic blood loss:[53,54] minimize number of blood draws and volume, minimize volume of blood	• Address clinically significant coagulopathy early by identifying the source and/or coagulation defect

		wasted (microtainers/small phlebotomy tubes) • Staging and packing • Interventional radiological embolization • Restrictive transfusion strategy[55-58] (Reduce volume of transfusion, adhere to restrictive transfusion thresholds) • Watch for signs of postop bleeding • Monitor throughout withholding/bridging/ recommencement of direct oral anticoagulants (DOACs) and antiplatelet agents • Prevent GI bleeding (enteral feeding/food, GI acid-lowering agents) • Avoid/treat infections promptly	
	• Identify patients and surgical procedures at increased risk for blood loss, anemia and coagulopathy • Refer high risk patients immediately to PBM program • Pre-operative surgical planning to minimize extent and time of surgery including preoperative embolization or non-invasive techniques • Postpone or cancel elective surgery to allow time to optimize blood health		

7. Standard Operating Procedures (SOP) and procedural guidelines	• Standard operating procedures (SOPs) for detection, evaluation and management of anemia and iron deficiency for specific settings:
	  • Pre- and post-surgery
	  • Cancer
	  • Heart failure
	  • Chronic kidney disease
	  • Pregnancy and postpartum
	  • Pediatrics
	  • Hospital-acquired anemia
	  • Patients with iron-restricted erythropoiesis
	  • Anemia of inflammation
		• Management of anticoagulants and antiplatelet agents prior to interventions
		• Bleeding history-taking
		• Bleeding management algorithms
		• Procedural guideline for cell salvage
		• Procedural guideline for ANH
		• Maintaining normothermia
		• Major hemorrhage protocol
		• Guidelines on oral vs inatravenous iron, iron preparations and dosing
		• Establish “single-unit transfusion policy”[59-62]	

8. Data collection, benchmarking and reporting systems	• Patient-centered and data-driven decision making • Measure the change with respect to patient outcomes/cost savings[63] • Report the change[64]		
9. Continuous education and training	• Multi-disciplinary and multi-professional programs organized and led by local champions • Regular updating of curricula/learning content • Ensuring introductory courses for new and junior staff		
10. Patient education, information and consent	• Develop a simplified education management plan • Establish procedures for communicating with patients re treatment plan, risks/benefits and obtaining consent[65] • Communicate plan to all members of the team		
11. Infrastructure	• Appoint PBM staff and allocate/reallocate funds accordingly[28] • Create job descriptions for PBM dedicated staff[28] • Install necessary medical devices and equipment[28,29] • Re-engineer clinical pathways and infrastructure to allow appropriate pre-operative/pre-intervention patient assessment and optimization[28,29] • Ensure appropriate waiting zones and treatment areas particularly for pre-operative/pre-intervention patient optimization[28] • Form a multi-disciplinary PBM committee[28]		

Table 2- Patient Blood Management (PBM) related guidelines and recommendations by specialty and/or clinical settings.

Setting	Guidelines
1. Massive hemorrhage	Patient Blood Management Guidelines: Module 1 - Critical Bleeding / Massive Transfusion. National Blood Authority, 2011[11] Management of bleeding and coagulopathy following major trauma: an updated European guideline, 2019[22]
2. Perioperative	Patient Blood Management Guidelines: Module 2 - Perioperative. National Blood Authority, 2012[12] Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: First update 2016[23] EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery, 2017[21]
3. Medical	Patient Blood Management Guidelines: Module 3 - Medical. National Blood Authority, 2012[13] Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines, 2018[24]
4. Intensive care/critical care	Patient Blood Management Guidelines: Module 4 - Critical Care. National Blood Authority, 2012[14]
5. Obstetrics and gynecology	Patient Blood Management Guidelines: Module 5 - Obstetrics. National Blood Authority, 2015[15] UK guidelines on the management of iron deficiency in pregnancy, 2012[25] Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement, 2018[17]
6. Neonatology and pediatrics	Patient Blood Management Guidelines: Module 6 - Neonatal and Paediatrics. National Blood Authority, 2017[16] Patient Blood Management for Neonates and Children Undergoing Cardiac Surgery: 2019 NATA Guidelines[18] Society for the advancement of blood management administrative and clinical standards for patient blood management programs, 2019[19,20]
7. Hospital PBM implementation	Supporting Patient Blood Management (PBM) in the EU - A Practical Implementation Guide for Hospitals, 2017[28]
8. State-wide PBM implementation	Building National Programmes of Patient Blood Management (PBM) in the EU - A Guide for Health Authorities, 2017[29]