CSL Behring

The new shape of coagulation

Moderators: Ravishankar Raobaikady and Diana Castro Pauperio

Thursday, April 24, 2025

1. REVERSAL OF DIRECT ORAL ANTICOAGULANTS: GUIDANCE FROM ISTH

Marc Samama

There are three ways to revert the effect of anticoagulants, especially direct oral anticoagulants (DOACs).

Reversion of anticoagulation	Type	Reverted anticoagulant
Drug removal 	· Dialysis · Antibody (Idarucizumab) · False target	· Dabigatran · Dabigatran · Dabigatran / FXa inhibitors
Drug absorption 	· Activated charcoal	· Dabigatran / Apixaban
Molecules with different mechanisms of action 	· Prothrombin Complex Concentrate (PCC) · Activated Prothrombin Complex Concentrate (aPCC) · Recombinant factor VIIa (rFVIIa)	· Dabigatran / FXa inhibitors · Dabigatran / FXa inhibitors · Dabigatran / FXa inhibitors

PCC

A meta-analysis published in 2019, including case series in a single arm, concluded that it is difficult to determine whether using PCC provides any benefit to the interruption of DOACs (FXa inhibitors) in patients with severe DOAC-related hemorrhage[1].

Percentage of patients with an effective treatment of severe hemorrhage:

IN 2 STUDIES WITH ISTH CRITERIA	IN 8 STUDIES WITHOUT ISTH CRITERIA
69% (95% CI, 61-76)	**77%** (95% CI, 63-92)

In a retrospective study assessing the efficacy and safety of PCC to revert apixaban/rivaroxaban before an emergency surgery, the following results were observed[2]:

- No patient required additional PCC
- **5%** of bleedings during the intervention
- **26%** of patients received cell concentrates
- **21%** of mortality within 30 days
- **3%** of thrombosis within 30 days

According to the *International Society on Thrombosis and Haemostasis* (ISTH)[3] four-factor PCC (4F-PCC) presents:

- Global efficacy **80%**
- **4%** incidence of thromboembolism
- Preventive efficacy in patients treated with DOACs without bleeding that must undergo an emergency invasive procedure
  - Comparative studies with placebo are required
- No differences between the fixed dose and the weight-based dose

aPCC

According to ISTH, aPCC[3] is associated with:

- Increases in thrombin generation higher than PCC or rFVIIa
- **56%** of patients with massive bleeding that achieve moderate-good hemostasis
- **84%** of patients undergoing emergency surgery that achieve Normal surgical hemostasis

rFVIIa

According to ISTH, there is no evidence supporting its use in patients with DOAC-related bleeding, and there are not enough concluding safety data[3].

IDARUCIZUMAB

- Its affinity for dabigatran es 350 times higher than for thrombin[4].
- 2.5 hours on average until the bleeding stops in patients with uncontrolled hemorrhage (intracranial or gastrointestinal)[5].
- 93,4% of patients with normal perioperative hemostasis before the emergency procedure[5].
- 6-7% thrombotic events[5].
- 19% mortality[5].

ANDEXANET ALFA

- Approved by the FDA with a safety warning, on account of its risk of thromboembolism, ischemia, cardiac arrest, and death.
- Efficacy after 2-5 minutes and short $T_{1/2}$ (1 h) ➡ the desired effect is achieved through continuous infusion + bolus[6].
- In a prospective open study, with a single group including 352 patients with predominantly gastrointestinal or intracranial hemorrhage, using questionable hemostasis criteria (primary outcome), the following results were observed[6]:
  - 82% of patients with excellent hemostasis 12 hours after infusion.
  - 10% of patients with thrombotic events within 30 days.
  - 14% mortality.
- Results vs Standard treatment[7]:

	Andexanet	Standard treatment
Hemostasis efficacy	67%	53,1%
Xa activity reduction	94,5%	26,9%
Thrombotic events	10,3%	5,6%
Ischemic stroke	6,5%	1,5%

- Better hemostasis control, but with no differences in the results at discharge vs. PCC[8].

CURRENT RESEARCH STRATEGIES

- Ciraparantag
- FXa variants

KEY MESSAGES:

- **DOAC reversion must consider both targeted drugs and clear stepped institutional strategies.**
- **Ciraparantag offers a promising option as a multi-specific reverter, although it clinical role is still under study.**
- **Designing rapid-action algorithms and setting up clinical teams are cornerstones for the modern management of bleeding under direct anticoagulation.**

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2. FACTOR XIII

Elisabeth Adam

FXIII is a thrombin-activated transglutaminase, and it is essential for clot stability, increasing its rigidity and providing resistance to proteins, as well as for wound healing[9]. FXIII not only stabilizes coagulation, but it also protects, repairs, and heals.

There are two types of FXIII deficiency (FXIII activity < 70%)[10,11]:

Congenital	Acquired
Homozygotes • 1-3 cases / 4 million • Experience bleedings **Heterozygotes** • 1 case / 1000 • Normally asymptomatic	1 case / 1000 **Causes:** • Burned/large wounds • Surgeries and polytrauma • Disseminated intravascular coagulation and sepsis • Liver parenchyma lesion / Cirrhosis • Cancer • Hematological / autoimmune diseases • Inflammatory bowel disease

It has been observed that FXIII availability per generated thrombin unit is significantly lower in patients with bleeding before, during, and after surgery[12], and that cancer patients with a high risk of intraoperative hemorrhage treated with FXIII during surgery experience less blood loss and use of fibrinogen than those treated with placebo[13].

FXIII deficiency often goes unnoticed, and standard analysis are not enough[14].

Quantitative tests (ELISA, chromogenic tests) are required to specifically determine FXIII deficiency.

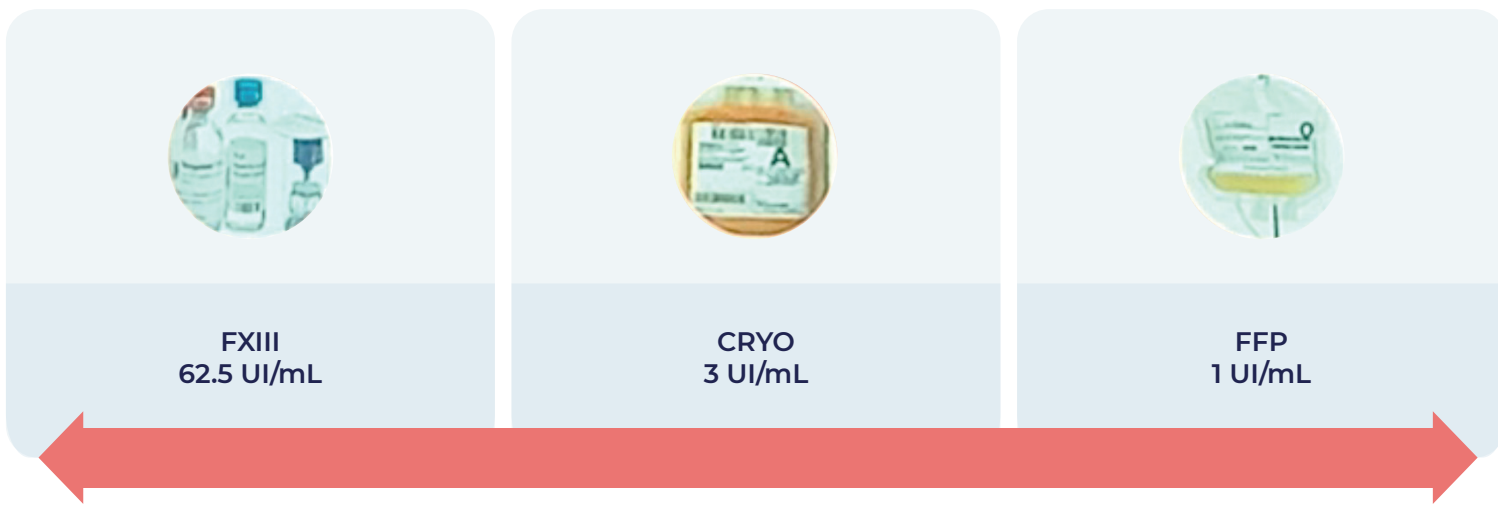
Standard coagulation tests	Many patients will present normal international normalized ratio (INR) and activated partial thromboplastin time (aPTT).
Viscoelastic tests	ROTEM, TEG, ClotPro may show FXIII deficiency, through the reduction of the clot rigidity, but they are not specific for FXIII determination.
Qualitative trials	A clot solubility test may be used, but the specificity is only shown in case of severe deficiency.

The *European Society of Anaesthesiology and Intensive Care* (ESAIC) suggests monitoring the FXIII and correcting the deficiency in case of a continuous hemorrhage not responding to the multimodal coagulation therapy or in critical patients presenting cicatrization defects (2C)[15].

- However, the use of FXIII is considered off-label in several settings, and it is indicated according to clinical judgment.
- Activity levels at which it should be administered vary between different authors, and a consensus is required on the desired levels[15,16].
- An FXIII concentration <60-70% may affect clinical results in trauma, surgery, and wounded patients.

FXIII DOSING:

10-40 UI/kg (20 UI, if tests cannot be performed and it is an empirical treatment). Considering FXIII concentration in each one of the available products, it makes sense to administer FXIII concentrate.



In summary, conducting tests and administering FXIII should be considered in high-risk patients.

KEY MESSAGES:

- **FXIII is essential for clot stability, but it is rarely assessed.**
- **FXIII deficiency should be suspected in persistent bleeding with normal hemostasis studies.**
- **Targeted replacement may have a relevant impact in complex hemorrhage contexts.**

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3. OLD AND NEW FIBRINOLYSIS INHIBITORS

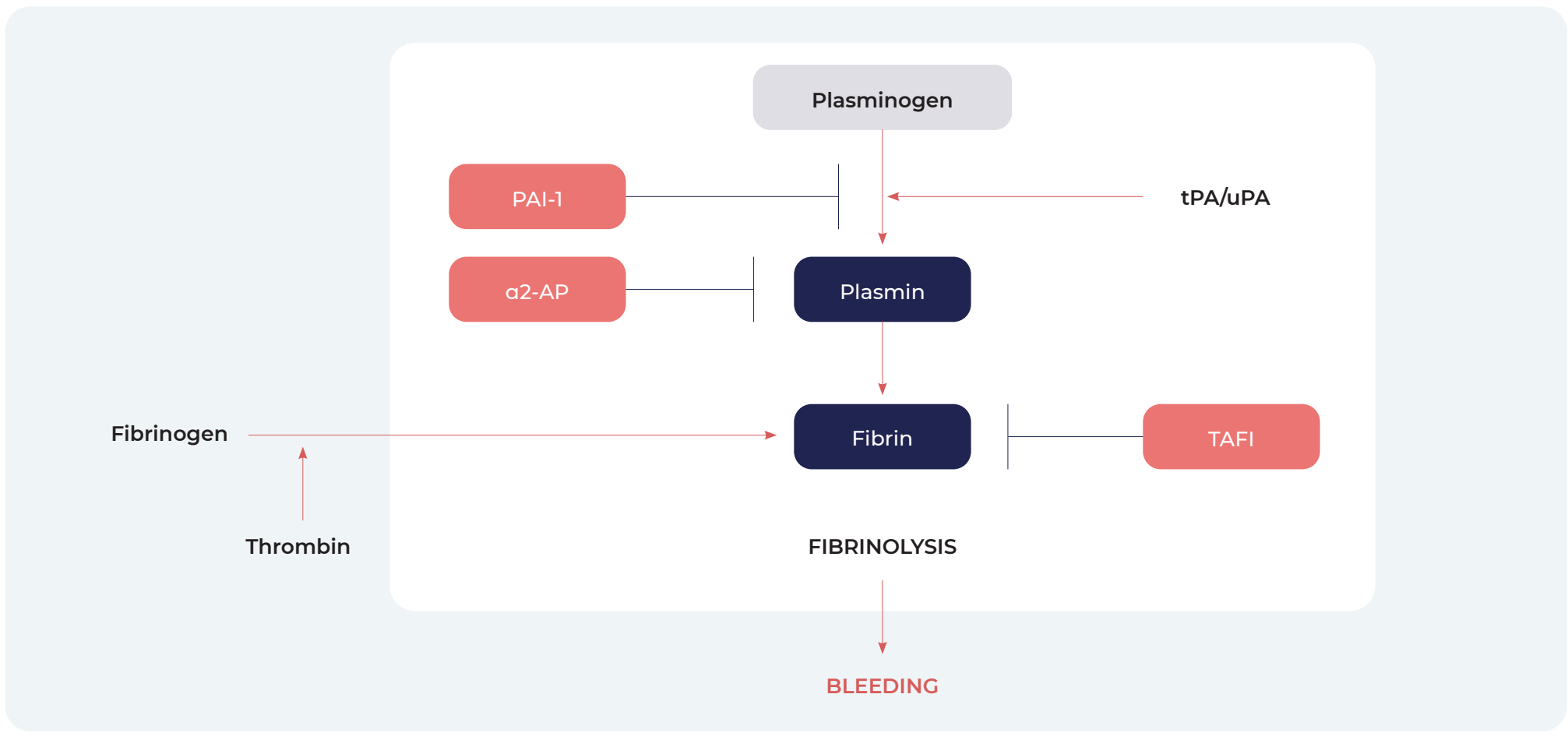
José Antonio Paramo

Acute hemorrhages are a significant health problem[17,18]:

Uncontrolled hemorrhage causes over a quarter of injury-related deaths and over 40% of post-injury deaths

Postpartum hemorrhage is still a frequent obstetric emergency and the main cause of maternal mortality worldwide

Hyperfibrinolysis appears as a result of an unbalance between pro- and antifibrinolytic molecules (due to situations such as surgery, trauma or delivery), and it can produce potentially-lethal hemorrhages in surgical and medical settings.



Antifibrinolytic agents used so far:

Aprotinin	Bovine pulmonary tissue isolate protein.
Tranexamic acid	Synthetic lysine analogue.
Aminocaproic acid	Synthetic lysine analogue.

TRANEXAMIC ACID

Tranexamic acid blocks plasminogen lysine binding sites, and thus it inhibits binding to fibrin and activation of plasminogen to plasmin. It also reduces fibrinolysis and stabilizes the clot[19].

Indications[20–22]:

- Trauma
- Postpartum hemorrhage
- Major surgery

Non-recommended use in[23]:

- Prevention of postpartum hemorrhage
- Gastrointestinal or intracranial hemorrhage
- Traumatic brain injury

Therefore, further safe antifibrinolytics need to be approved to manage patients with major bleeding.

CM-352

CM-352 is a new molecule with a new mechanism of action (pan-MMP inhibitor) that inhibits fibrinolysis and proteolysis[24,25].

0.7 nM concentration → 50% delay in lysis time[26]

T1/2 = 1,4 h → It allows effect regulation during infusion[26]

PRECLINICAL RESULTS:

- Significant reduction of bleeding time compared to control and to tranexamic acid and aprotinin, in a hyperfibrinolytic model[26].
- Significant reduction of blood loss compared to control in a hepatectomy model, whereas tranexamic acid and aprotinin cannot get there[26].
- Reduction of hematoma expansion and lesion volume after 3 and 24 hours in an intracranial hemorrhage model, both with early (1 hour) and late (3 hours) administration[27].
  - Reduction of sensorimotor development
  - Reduction of neurological deficit
- Very effective in controlling rivaroxaban-related intracranial hemorrhage[27].
- Reduction of the number of neutrophils in the hemorrhage area[27].

In summary, CM-352 presents a great bleeding control potential in surgical and medical settings, including intracranial hemorrhage cases.

KEY MESSAGES:

- **Tranexamic acid is effective, but not universally applicable or risk-free.**
- **New antifibrinolytics seek more molecular specificity with less toxicity.**
- **Fibrinolytic phenotype identification will be key for hemostasis personalized medicine.**

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Patient Blood Management in Acute Care and Critical Illness: A Process Map for the Future

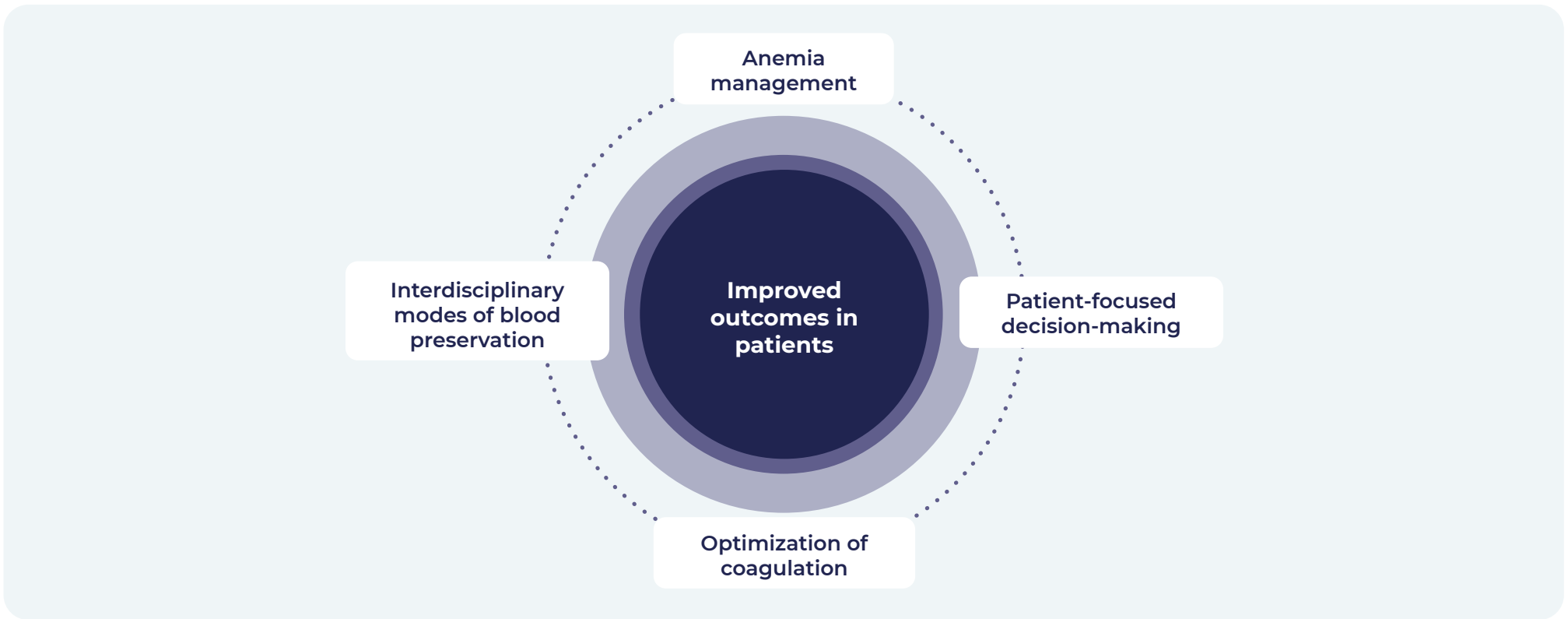
Moderators: Sigismond Lasocki and Patrick Meybohm

Friday, April 25, 2025

1. TRAINING OUR FUTURE LEADERS: WHAT ANESTHESIOLOGISTS AND CRITICAL CARE PHYSICIANS SHOULD KNOW ABOUT TRANSFUSION MEDICINE

Gagan Mathur

Transfusion medicine brings together clinical experience (blood collection, transfusion, apheresis, and cell therapy), biochemistry, and the regulatory perspective. The current trend includes management and preservation of the patient's own blood, while promoting their safety and empowerment. For that purpose, it is required to get away from the transfusion-focused approach and closer to a more holistic, patient-focused, systematic, evidence-based model[1].



The final goal of *patient blood management* (PBM) is to ensure the optimal functionality of all blood components of each individual and their interactions with all other organs and systems[2].

However, a system-wide change is needed because there are several barriers for the implementation of PBM:

- Suboptimal anemia management
- Transfusion-centered culture
- Limited patient involvement
- Fragmented interdisciplinary cooperation

Given that scarce interdisciplinary cooperation hinders the implementation of PBM, training future leaders and setting up interdisciplinary teams is necessary, in order to promote harmonized practices, reinforce the effectiveness of programs, and to improve patient care in all departments.

Transfusion medicine acts as a bridge between the clinical and operational settings. These are the three basic pillars for its implementation:

EDUCATION

Education in the following aspects is essential to enable the healthcare team and to implement an evidence-based PBM:

- Reinforcing best practices related to transfusion thresholds, anemia, coagulation, and goal-directed therapy.
- Educating students, residents, interns, and healthcare professionals in the principles of PBM.
- Educating nurses on the reduction of the phlebotomy, transfusion safety, and early detection of anemia.

DATA GENERATION AND ANALYSIS

Generating robust data is required for a successful implementation of PBM:

- Driving the implementation of PBM and monitoring its performance.
- Harnessing electronic records (lab as a source of data).
- Access and resources (for regulatory and qualitative purposes).

LEADERSHIP

Leadership is essential to implement PBM at an institutional level:

- Generating clinical practice guidelines and protocols.
- Configuration of expert committees and working groups.
- Fostering a cultural shift based on data use, commitment, and education.

KEY MESSAGES:

- **Transfusion medicine should be taught as a cross-discipline skill from the residence.**
- **PBM leadership requires technical knowledge, management skills, and educational ability.**
- **There are international programs that may be used as a model for Europe.**

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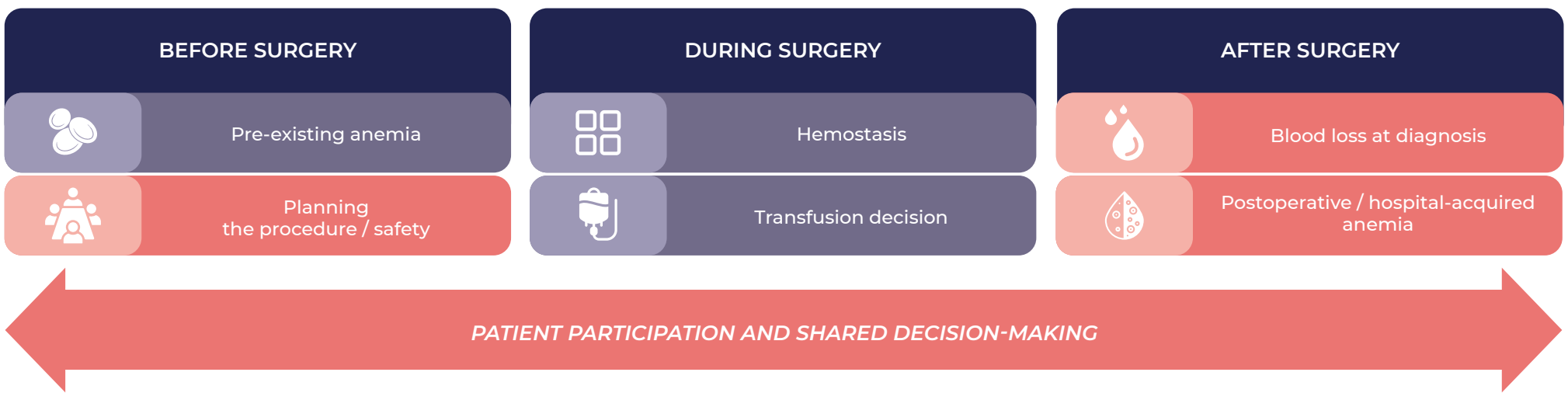
2. PATIENT BLOOD MANAGEMENT IS THE FUTURE OF ACUTE CARE AND PATIENT RECOVERY

Matthew Warner

PBM is an intervention carried out at three specific times. The goals are different at each one of them[3]:



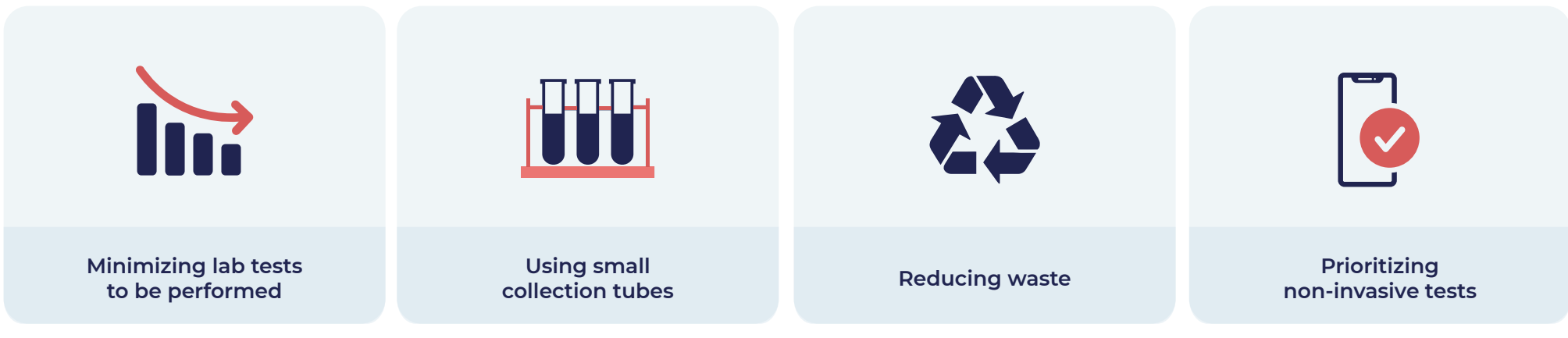
Next, different strategies are defined to achieve each one of the four goals on which the presentation is focused, as well as to reinforce the patient participation and shared decision-making between the patient and the clinician.

1. PROCEDURE PLANNING

- Team work is a must.
- The use of technology can help improve clinical outcomes.
- Patients should get involved in decision making.

2. BLOOD LOSS AT DIAGNOSIS

Anemia is frequent in critical patients, and it may get worse due to phlebotomy-related iatrogenic blood loss. Each 100 ml of phlebotomy volume during hospitalization is associated with a 15% increase in transfused red blood cell units. In fact, patients in the top quartile of cumulative blood collection experience the highest transfusion rates[4].



An optimized blood collection tube program may entail a 41% reduction in collection tubes, and $25,000 in related costs, a 59% decrease in collected blood, and 1,071 L of blood saved every year[5]. The use of small tubes has also been reported to entail a decrease in red blood cell transfusion, with no impact on the number of collected insufficient samples[6].

3. POSTOPERATIVE ANEMIA

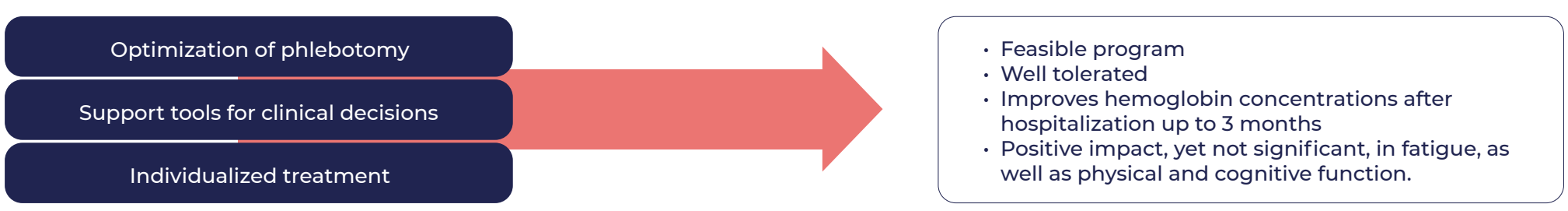
Postoperative anemia is common yet not benign, and it involves a number of significant consequences:

- A decrease of 1 g/dL in hemoglobin at hospital discharge produces a 10% increase in the risk of re-admission within 30 days[7].
- Postoperative anemia has an impact on survival, which is dependent on hemoglobin concentration[8].
- Recovering 1 g/dL within a month entails a 13% decrease in the re-admission risk, and an 18% reduction in the risk of death[9].

Intravenous iron is a potential treatment, although there are not enough studies available yet and its effect on the transfusion rate or the clinical outcomes is not very conclusive[10–12].

IV Fe	• Increases Hb • It may reduce the number of transfusions and improve relevant outcomes for patients

The results of a study were recently published assessing the effect of a multifaceted anemia control program on the recovery of hemoglobin after hospitalization and on the functional results in survivors of acute diseases[13].



4. PATIENT PARTICIPATION AND SHARED DECISION-MAKING.

A study in the United Kingdom assessed the practice of obtaining informed consent for blood transfusion, observing it only occurred in 43% of cases[14]. Both patients and clinicians declared having discussed or mentioned the following items:

	Patients (n=2243)	Clinicians (n=1633)
Discussion of transfusion	76%	85%
Mention of risks	38%	38%
Mention of alternatives	8%	14%

Another qualitative study with preoperative patients concluded that discussions on transfusion are superficial, and that some patients would rather delegate decision making to the medical team, whereas others consider their preferences should be included, but most patients are willing to participate in strategies to reduce the number of transfusions[15].

KEY MESSAGES:

- **PBM is applicable and necessary in critical patients, not only surgical ones.**
- **Transfusion should be a reasoned exception, not a default response.**
- **Implementing PBM in the ICU improves clinical outcomes, costs, and healthcare safety.**

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3. MOVING THE NEEDLE IN CARDIAC SURGICAL PROCEDURES

Linda Shore-Lesserson

The results of a study published in 2008 concluded that there is a significant variability in perioperative transfusion practice in the context of cardiac surgery between sites from different countries[16]. Another study published in 2010 also described a wide variability in transfusion rates of red blood cells and other blood products between patients undergoing coronary artery bypass surgery with cardiopulmonary bypass in hospitals in the United States[17]. This variability may be due to differences in practice patterns, as well as a potentially inappropriate use of transfusion.

The *Society of Thoracic Surgeons* (STS) and the *Society of Cardiovascular Anesthesiologists* (SCA) published a set of guidelines for preoperative transfusion and blood preservation in cardiac surgery in 2007[18]. Adherence to such guidelines was subsequently studied and a wide variability was observed in current practices of preoperative, perfusion, surgery, and pharmacological testing, and the following results were obtained[19]:

- Institutional discussion after checking guidelines **20%**
- Institutional action after checking guidelines **14%**
- Change in practice which was effective in the reduction of transfusion rates **26%**
- The adherence to recommendations on the use of erythropoietin did not reach **30%**

When the mentioned guidelines were updated in 2011, they included quality measures related to four recommendations in class 1, 100%-compliance of which leads to certification[20]:

- Use of lysine analogues
- Use of minicircuits or retrograde autologous priming or ultrafiltration volume
- Use of *cell salvage*
- Use of algorithm and test at the point of care

Later on, Joshi et al. published the results obtained from a study with 30-item questionnaire assessing adherence to measures in *Anesthesia Quality Institute's* (AQI49)[21], leading to the following results:

WIDESPREAD ADOPTION OF BEST PRACTICES ON:

- Lower tolerance to hemoglobin
- Antifibrinolytics
- Minimizing hemodilution
- Cell salvage

IDENTIFICED BREACHES:

- Preoperative anemia management
- Use of algorithms and tests at the point of care

HIGHER ACHIEVEMENT IN ALL 4 CRITERIE IN SITES WITH PBM MULTIDISCIPLINARY TEAMS.

When the guidelines were updated in 2021, they included certain developments, such as the recommendation of assessing anemia and the determination of its etiology in all patients undergoing cardiac surgery, as well as treatment with intravenous iron if time allows[22]. This recommendation may go a little further in future editions.

The guidelines of the *European Association for Cardio-Thoracic Surgery* (EACTS) and the *European Association of Cardiothoracic Anaesthesiology and Intensive Care* (EACTAIC), published in 2024, already provide specific recommendations for PBM before admission, before, during, and after surgery[23]. For the first section, the following recommendations are put forward, among others:

Identification of anemia, causes and appropriate treatment (I-B).

- **Oral iron supplementation in patients with Hb < 120-130 g/L (IIa-B)**
- **Intravenous iron supplementation in patients with Hb < 120-130 g/L (IIa-A).**
- **Erythropoietin (IIa-A).**

Last, in 2025, the recommendations generated in a consensus on bleeding control and transfusion management were published, including qualitative measures suggested in cardiac surgical bleeding[24]. These are the new items in the guideline:

- Universal definition of excessive bleeding soon after surgery.
- Production pressure as a non-measured bleeding risk factor.
- Immediate reexploration for bleeding to reduce risk of adverse results.
- Quality indicators should be expanded beyond reexploration rates, comprising factors such as surgical bleeding *checklists* and time to reexploration.
- Individualized assessment of risks and benefits of discontinuing or not anticoagulant and antiaggregant treatment.

KEY MESSAGES:

- **Cardiac surgery is the paradigm where PBM shows a higher clinical impact.**
- **Viscoelastometry allows for rational guided hemostatic replacement.**
- **Developing protocols for PBM in major surgery is feasible and it is associated to less transfusions and better prognosis.**

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The Digital Revolution in Patient Blood Management: The Future is Now!

Moderators: Andrea Steinbicker and Elvira Bisbe

Friday, April 25, 2025

1. PATIENT BLOOD MANAGEMENT IN THE DIGITAL AGE: OPTIMISING OUTCOMES THROUGH INNOVATIVE APPROACHES

Diana Castro Pauperio

There are tech companies that can provide support to digitize hospital processes, such as *patient blood management* (PBM). In Portugal, the Local Health Units in Gaia/Espinho, Matosinhos, and Tamega and Sousa have started the digitization of the journey of patients receiving PBM to achieve value-based care and practices, which has been ongoing since March 2024.

The steps in this process were the following:

1. OPERATIONAL AND INFORMATION MAPPING: WHAT VARIABLES ARE COLLECTED

Operational	Information
· Appointments · Treatments · Tests · Teams · Infrastructure	· CROMs · PROMs · PREMs · Financial information

PROMs, Patient-Reported Outcome Measures; CROMs, Clinician-Reported Outcome Measures; PREMs, Patient-Reported Experience Measures

2. *PATIENT JOURNEY* DIGITIZATION

Subsequently, the tech company may provide different types of data:

Identifiable data	Anonymous data
· At patient level · At patient-group level · Existing platforms in hospital/systems	· Research · Existing platforms in hospital/systems · Decision-making: local administration, pharmacy directors, or clinical directors

The goals set were the following:

- **Decreasing the work load**
- **Efficacy and efficiency of interventions in PBM**
- **Identifying unmet needs**
- **Assessing the adherence of patients to digital tools**
- **Generating data in real-life clinical practice**
- **Determining standard collection of certain PROMs and CROMs**

CROMs are also predetermined and organized in three dimensions, but each site can apply them as they see fit. PROMs have also been predetermined to the convenience of each site, and they are offered in several languages.

Once the patient journey has been generated, processes such as sending educational contents to patients or collecting quality of life measures are automated. The system also determines the assessments that should be performed after surgery and at what time.

The changes experiences since the digitization of the process are the following:

- Exponential increase of data in real-life clinical practice available in one year and dynamic analysis.
- Better monitoring of patients.
- Cost-saving per patient.
- Improved patient adherence
- Operational optimization.
- Increase in clinician motivation.
- Identification of unmet patient needs through the collection of PROMs.
- Obtaining information at individual and global level.
- Decrease in the use of packed red blood cells, platelets, and fresh frozen plasma.

Therefore, PBM in the digital era is possible and achievable, and technology makes customized medicine possible.

KEY MESSAGES:

- **Digitization allows the integration of PBM in clinical flows in a non-intrusive effective way.**
- **Systems must work as active clinical assistants, not just as data repositories.**
- **Hospital system interoperability is critical for PBM continuity.**

CSL Behring

The Digital Revolution in Patient Blood Management: The Future is Now!

Moderators: Sigismond Lasocki and Patrick Meybohm

Viernes, 25 de abril de 2025

2. MACHINE LEARNING AND PBM

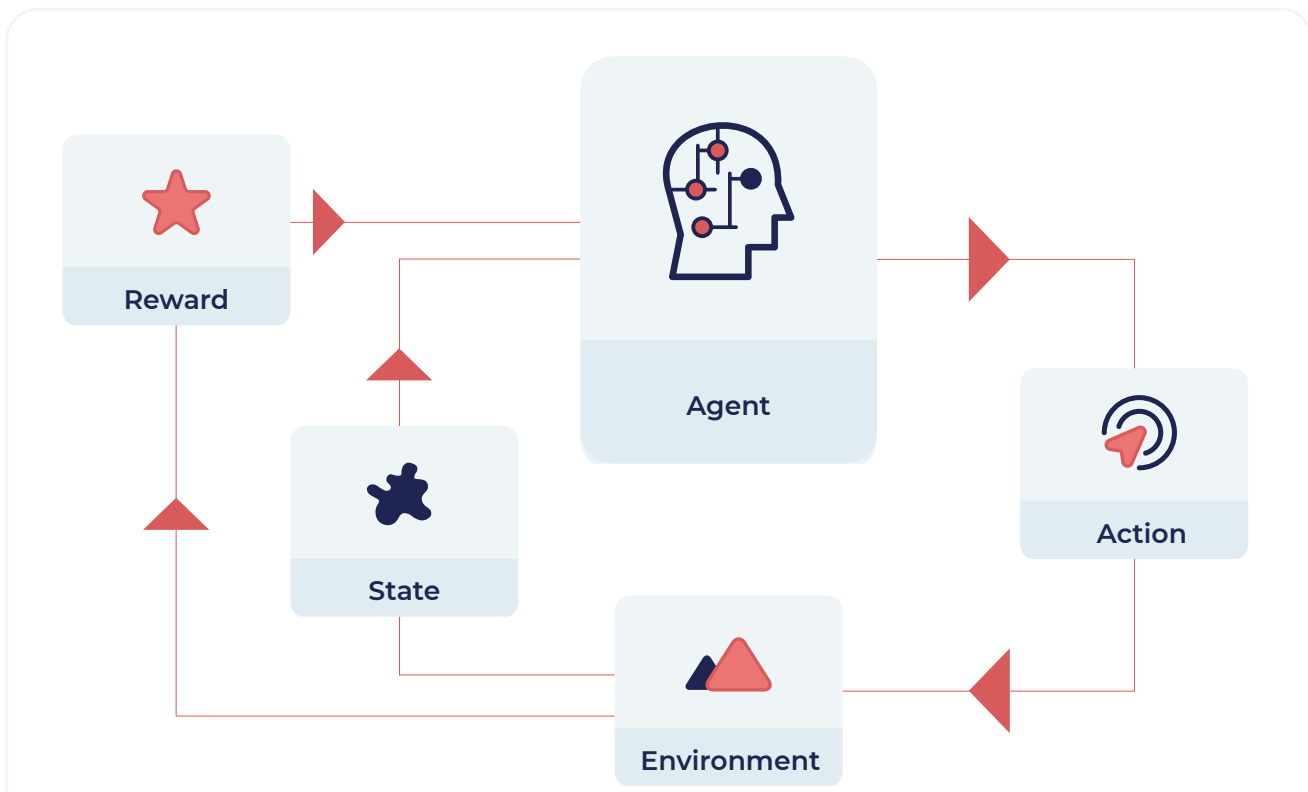
Jens Meier

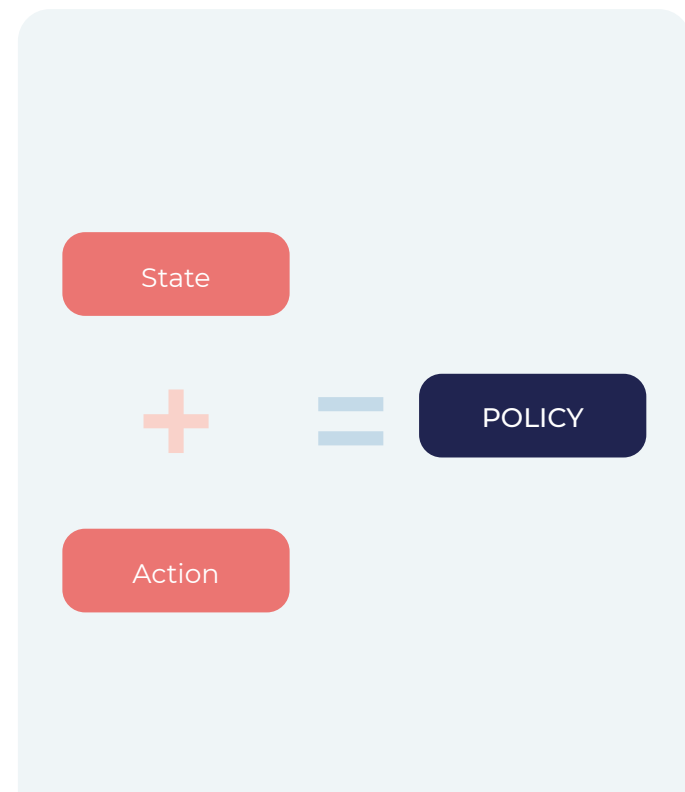
Currently, there are many publications on models predicting whether a patient will be transfused or not. However, in the context of transfusion, the goal would be for artificial intelligence (AI) tools to help decide whether a patient should be transfused or not.

If we use AI tools, such as CHATGPT, then chances are that, in certain clinical settings and when doubts arise, the answers given come from clinical practice guidelines. Nevertheless, we know that guidelines are crude generalist tools not providing bespoke solutions. Additionally, these documents have been drafted from evidence-based medicine and, occasionally, from expert opinions.

In real-life clinical practice, each patient is unique, with specific comorbidities, and so it is each clinical situation. The same clinical decision, made respecting and following the guidelines, may have completely different outcomes in each patient, depending on their path and circumstances.

Taking all of this into account, the new paradigm is reinforcement learning, a field within AI which is about building systems that learn from data to make predictions and decisions. This is a type of automated learning in which an agent learns to make decisions with trial and error, while interacting with the environment to maximize the reward. In this framework, a policy is the strategy applied by an agent to decide what action to adopt in each state of the environment.





Automated learning models are well established in transfusion prediction, but not yet to determine whether a patient should receive a transfusion.

In the future, large language models (LLM) will be able to guide transfusion decisions, and reinforcement learning is the path to achieve that goal.

A model designed with patient data collected in the *Medical Information Mart for Intensive Care IV* (MIMIC-IV) and in the eICU database is presented. It includes different variables (age, gender, *International Classification Diseases*, lab values, etc.), and it assesses the outcome of having used hemoglobin concentration as a policy:

Permite minimizar la transfusión

Sin efecto en la supervivencia

However, reinforcement learning still poses several challenges:

- Environment-state formulation.
- Formulation of actions.
- Reward design.
- Assessment: confidence in simulations and assessment methods.
- Roll-out in the production environment:
  - Shortage of clinical trials
  - Safety guidelines for real-world implementation

KEY MESSAGES:

- **Machine learning can anticipate transfusion-related needs and risks better than isolated clinical assessment.**
- **It is essential to validate models in local populations and to keep them up to date with recent data.**
- **Artificial intelligence cannot replace clinical judgment, but it can amplify it and reinforce it.**

The Digital Revolution in Patient Blood Management: The Future is Now!

Moderators: Sigismond Lasocki and Patrick Meybohm

Friday, April 25, 2025

3. DATA SCIENCE: THE NEXT REVOLUTION IN PATIENT BLOOD MANAGEMENT

Kevin Trentino

The work of data managers is increasingly demanded. AI is increasingly popular in business, and companies feel they need this role to develop AI models[1]. The future of medicine will integrate patient care with constant remote monitoring of patients, both at the hospital and at home. All these data can be integrated and analyzed.

Early medical alert systems that will be implemented in the future are the following[2]:

- **Systems based on AI and automated learning**
- **Electronic clinical history, Real-time hemodynamic monitors**
- **Real-time hemodynamic data**
- **Cognitive data**
- **Surgery and OR video monitoring**
- **Social-economic and racial/ethnic determinants of health**
- **Genetic testing and precision medicine**

Predictive models in medicine are increasingly more relevant in PBM. However, most transfusion predictive models entail a high risk of bias in their development and validation (participant selection, predictive factors, result, and analysis), and start from poor information and methodological quality. These aspects should be tackled before they can be safely used in clinical practice[3].

Present limitations are the following:

- Data quality
- Overadjustment
- Transparency
- Relevance

In 2008, the Western Australian Department of Health started a holistic PBM program. During the early stages, data were collected and it was observed that feedback was fundamental for the program to succeed. In 2013, an article was published describing the associated PBM data system, and proving its usefulness to monitor transfusions practices and the use of the product in the framework of a PBM pilot program[4]. Models such as this may help effectively guide PBM strategies, as well as continuously monitor its impact. A subsequent publication described the development of totally automated control panel revolving around three key indicators: transfusions of single red blood cell unit, transfusions to patients with hemoglobin >8g/dL, and elective surgery patients admitted with anemia. Further indicators may be added depending on the needs. These panels may allow comparison between clinicians, departments, and even hospitals[5].

Other studies have shown that the need for in-hospital transfusion, unlike the amount of red blood cell units transfused during a hospital stay, may be predicted reliably[6,7].

In summary, AI an automated learning models can improve patient care and the selective use of resources, but their current methodological quality must improve significantly.

KEY MESSAGES:

- **Thanks to data science, PBM performance can be monitored and improved at a population level.**
- **Displaying data transforms clinical behavior better than coercive policies.**
- **Clinical teams should lead the interpretation and application of the generated data.**

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CSL Behring

Shaping the future of PBM: Global guidance and innovation

Moderators: Sigismond Lasocki and Patrick Meybohm

Friday, April 25, 2025

1. FUTURE OF TRANSFUSION MEDICINE

Markus Mueller

Dr. Müller approached the future of transfusion medicine from an integrating perspective, combining scientific breakthroughs, digital transformations, and bioethical challenges.

He started his presentation by analyzing the limitations of the classic transfusion model:

- Late reaction: transfusion is applied once anemia has developed, not as a preventive measure.
- Lack of personalization: transfusion thresholds are only based on hemoglobin, regardless of the blood volume, inflammatory profile, or organic function.
- Poor traceability of clinical justification and subsequent effects.

He reckoned that the future of transfusion medicine should include:

- **Precision medicine:** algorithms integrating biomarkers, clinical data, and predictive tools in order to decide when and how to transfuse.
- **Intelligent automation:** blood bank platforms connected to the patient's clinical and surgical history, to suggest specific components or prevent selection errors.
- **Rational preservation:** inventory management strategies to minimize expirations, waste, and costs, particularly in platelet or irradiated components.

He also spent some time discussing **transfusion ethics**, including:

- The need for a real non-routine informed consent.
- The impact of overtransfusion as an unregistered iatrogenesis.
- The importance of hospital policies limiting unjustified variability between professionals and services.

He concluded arguing that transfusion medicine must transcend its logistic model and take on a proactive role within the healthcare process, integrating artificial intelligence, outcome-based medicine and value-focused institutional policies.

The TRICC clinical trial was the first one to determine that a restrictive red blood cell transfusion strategy was, at least, as effective as the liberal strategy[1], although there can actually be significant differences between the highly-selected population in the study and real-life patients[2].

When making decisions, it is important not to extrapolate the results of clinical trials to any type of patient.

A correlation between both events or observations does not involve causation. In the field of transfusion, results from retrospective observational studies are often published concluding there is a causal relationship between received transfusions and certain clinical outcomes, but such conclusions cannot actually be drawn from this type of studies.

In the FOCUS randomized controlled study, that included patients with a history or risk of cardiovascular disease and low concentrations of postoperative hemoglobin, no statistically significant differences were observed in mortality after 3 years of follow-up (secondary variable in the study) or in the causes of death between patients transfused following restrictive or liberal strategies[3].

To draft evidence-based recommendations in the Frankfurt consensus document on *patient blood management* (PBM), a thorough literature search was carried out, but eventually under 1% of the studies found were analyzed, which is a very low ratio[4]. Moreover, many of the recommendations were strong but backed by a moderate to low evidence level.

The demographic changes occurred in the last few years and the ones ahead will have an impact on the blood supply. In Germany, *babyboomers* (50-65), who currently account for most blood donors, will move on to the highest-receiving group in the next few years[5].

The number of donations per year in Germany is close to 2, which is relatively higher than other European countries. However, the donor ratio is low (3%), considering that 30% of the population could be donors. The average age of German donors is high (46.5), as well as that of new donors (32.9), and the donor return ratio after the first donation is only 25%.

B*lood farming* is proposed as a potential solution to the future blood shortage, but many unsolved issues lay still ahead.

Drawbacks of *blood farming*	Immortalization of direct reticulocyte precursors
• Long expensive differentiation process • Inefficient enucleation • Fragile reticulocytes	• Reduction of differentiation • Culture needed for terminal differentiation

These are the current challenges to ensure supply:

- Young donor motivation and commitment
- Donor mobilization in urban areas
- Yearly supply of all products
- Suppress perception of risk from blood

KEY MESSAGES:

- **Transfusion medicine must evolve into a more proactive, intelligent, ethical model.**
- **Automation and the use of artificial intelligence may increase transfusion safety.**
- **Unjustified transfusion variability should be considered a threat to healthcare equity.**

CSL Behring

Shaping the future of PBM: Global guidance and innovation

Moderators: Sigismond Lasocki and Patrick Meybohm

Friday, April 25, 2025

2. WHO GUIDANCE ON IMPLEMENTING PBM TO IMPROVE GLOBAL BLOOD HEALTH

Axel Hofmann

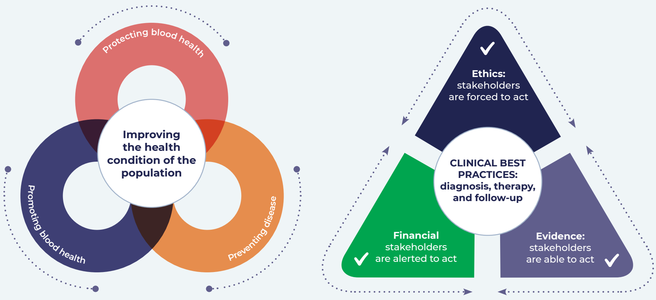
The World Health Organization (WHO) declared that PBM should be urgently implemented worldwide to improve patient clinical outcomes, promote safety, and cut costs, particularly in the inverted pyramid demographic context of the next few decades.

The recent publication of the document *Guidance on implementing patient blood management to improve global blood health status*[6] is a tool to include PBM in the public health agenda of all member states, and thus reduce the costly dependence of transfusions and reassign the limited funds to where they are most needed.

IMPROVING BLOOD HEALTH IS A GLOBAL PUBLIC HEALTH PRIORITY.

The document uses «model 8», a structured way for the implementation of complex integrated systems in large sectors. The model also integrates the «3Ps» and «3Es».

3P83E



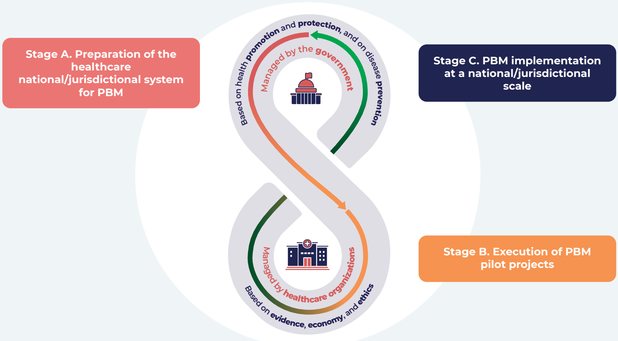
Human blood is also defined as an organ, since it meets all the criteria to be considered as such, although it is often dealt with as a connective tissue, a merchandise, a medication, or a replacement fluid.

HOW CAN THE DOCUMENT HELP OVERCOME CHALLENGES TO GLOBAL IMPLEMENTATION OF PBM

The document provides two essential tools:

- Path for national/jurisdictional implementation.
- PBM toolkits for specific patient populations and diverse resource levels.

PATH FOR NATIONAL/JURISDICTIONAL IMPLEMENTATION BASED ON MODEL 8



Stage A. Preparation of the healthcare national/jurisdictional system for PBM

1. Adopting a PBM policy.
2. Setting up governance for the implementation of PBM.
3. Anchoring the PBM in the WHO quality and safety framework.
4. Training professionals and students on the PBM.
5. Educating the public in matters of blood health.
6. Ensuring access to essential drugs and devices for PBM.
7. Allocating resources to PBM.
8. Selecting PBM pilot projects.

Stage B. Execution of PBM pilot projects

9. Having "champions" promote PBM in healthcare organizations.

> **"Champions" are individuals who support, advocate, and spearhead an implementation initiative, and who overcome resistance so that it can reach the whole organization. They have an inherent interest in implementing change, and they use their position to motivate others. They have good communication and tutoring skills to facilitate the acceptance of the initiative[7].**

10. Preparing the implementation of PBM in healthcare organizations by "champion" teams.
11. Authorizing the pilot project by the direction of healthcare organizations.
12. Creating a specific PBM structure for healthcare organizations.
13. Implementing specific PBM processes for each healthcare organization.
14. Setting up a PBM data and report collection system.

Stage C. PBM implementation at a national/jurisdictional scale

15. Selecting pilot sites as national references.
16. Collecting data, reporting, and *benchmark* the PBM results.
17. Fostering the certification of multidisciplinary physicians in PBM.
18. Fostering the certification and auditing of PBM programs.
19. Facilitating and funding PBM research and development.

PBM TOOLKITS FOR SPECIFIC PATIENT POPULATIONS AND DIVERSE RESOURCE LEVELS.

- Toolkits are a collection of resources, guidelines, strategies, and interventions designed to deal with specific health issues, improving patient care, and expanding the knowledge and skills of healthcare professionals.
- They are included in Appendixes 6-11 of the document. They are organized as tables to facilitate care to the following patients:
  - Anemia/iron deficiency
  - Hemorrhages and blood loss
  - Coagulation and hemostasis disorders
- They cover a wide array of issues and they are meant to be practical tools to implement PBM as a standard of care.
- They are organized based on the resource level:
  - Low-income countries
  - Medium-low and medium-high income countries
  - High-income countries
- They are targeted at specific populations:
  - Neonatology and pediatrics
  - Obstetrics
  - Traumas
- They are designed to reduce the difficulties when implementing PBM, increase the understanding and commitment of patients and healthcare professionals, and improve healthcare outcomes.
- They supplement steps 3 to 6 of the implementation managed by governments, but particularly step 13, aimed at organizations.

KEY MESSAGES:

- **La 2024 WHO guide legitimizes PBM as a healthcare policy.**
- **PBM is no longer a clinical initiative, but a global strategy against anemia and inappropriate transfusion.**
- **The "hospital" approach needs to shift to sustainable and auditable population models.**

LITERATURE

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