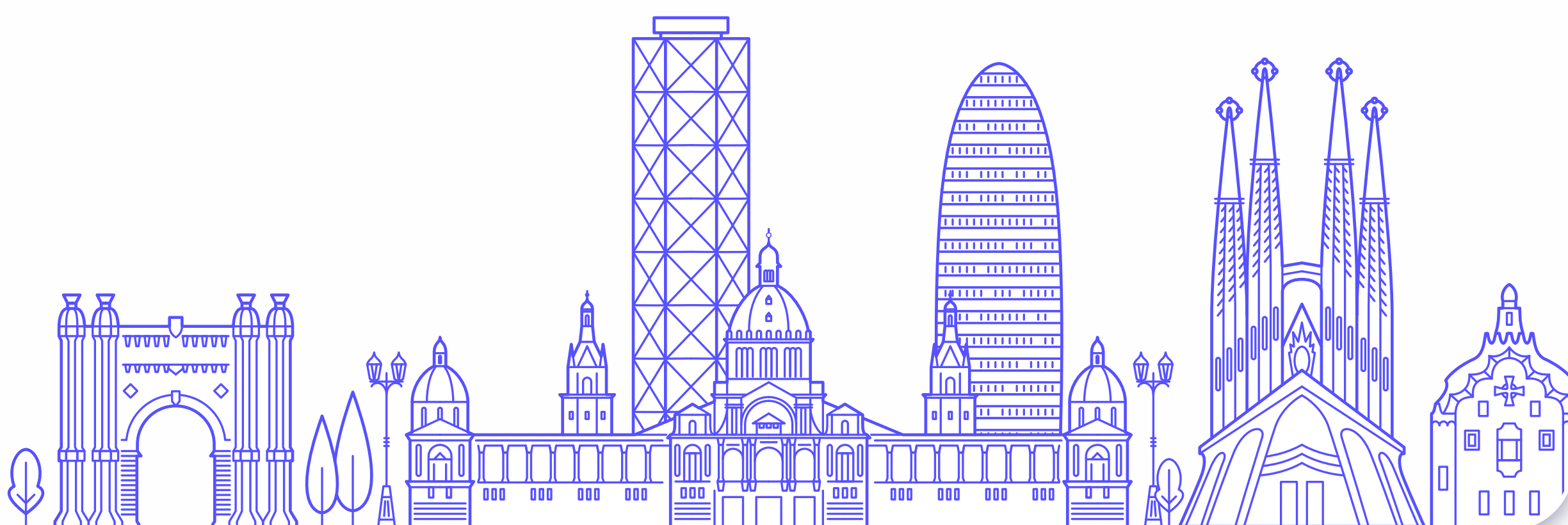


PBM ESSENTIALS

Patient Blood Management: THE ESSENTIALS

Summaries of key aspects of PBM
which were presented at the
PBM Masterclass 2025



The benefits of PBM over the standard of care

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What is Patient Blood Management?

PBM is a multidisciplinary, patient-centered, systematic approach that uses evidence-based medical and surgical methods to **improve patient outcomes by managing and preserving a patient's own blood**, while promoting patient safety and empowerment¹⁻³

- ✓ **PBM provides a framework to address the risks of iron deficiency, anemia, blood loss, and coagulopathy³**

PBM objectives are described in three pillars:²⁻³



Pillar 1

Detection and management of anemia and iron deficiency



Pillar 2

Minimization of blood loss and optimization of coagulation



Pillar 3

Leveraging and optimizing the patient-specific physiological tolerance of anemia

Why is PBM needed?

The prevalence of anemia and blood loss is high³



Anemia and/or micronutrient deficiencies

>2.9 billion

Chronic or acute blood loss and/or bleeding disorders

>600 million

Preoperative anemia increases perioperative transfusion needs^{4, 5}



Blood product transfusions are associated with **poor patient outcomes**, including:^{1, 6-8}



Risk of complications and mortality



Further bleeding

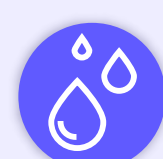
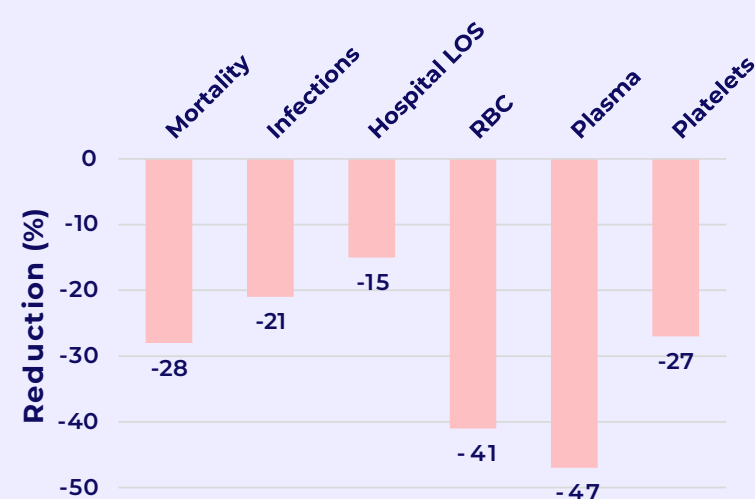


Longer hospital stays

Major bleeding, transfusion, and anemia are independent **risk factors** of significantly increased **morbidity, mortality, and hospital stays** in surgery settings^{1, 6-7}

PBM improves patient outcomes and reduces healthcare costs

A large retrospective study in >600,000 patients found that **following health-system-wide PBM implementation, patient outcomes and transfusion rates improved with reduced costs** over 6 years⁹



PBM implementation led to **significantly reduced preoperative anemia**, from ~21% to ~14% (p=0.001)⁹



PBM implementation led to **product-acquisition costs savings** of US\$ 18 M and **activity-based savings** of US\$ 78–97 M⁹

Likewise, a meta-analysis of 17 PBM programs found that their implementation significantly reduced:¹⁰

↓ Transfusion rates 39%	↓ Number of complications 20%	↓ Hospital LOS 0.45 days	↓ Mortality rate 11%
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PBM in trauma



Approximately one-third of patients with severe trauma are coagulopathic at hospital admission, and bleeding with coagulopathy is a leading cause of mortality¹¹

In major trauma, the use of **goal-directed coagulation and transfusion protocols** improved patient outcomes and transfusion needs compared with traditional management:¹²

- **Improved mortality and ICU LOS**
- **Reduced allogeneic blood product use**



PBM in obstetrics

PPH affects ~8.4 million women each year and is a leading cause of maternal morbidity and mortality worldwide^{3, 13}

A large international RCT found that compared with standard care, **early detection of PPH and use of a PBM-aligned treatment bundle** led to:¹⁴

- **Increased detection of PPH**
- **Reduced risk of severe PPH, laparotomy, or maternal death**

There is an urgent need for PBM implementation to improve patient outcomes, which provides an additional benefit of healthcare cost savings³



The WHO has provided comprehensive guidance on PBM implementation¹⁵



The WFSA has also endorsed PBM implementation¹⁶

Optimizing patient management with PBM protocols: Improving outcomes and saving costs

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Importance of medical protocols*

A medical protocol is a **diagnosis-specific** or **problem-oriented** written statement of **standard procedure or algorithm**, adopted by medical staff of a hospital/institution as the appropriate standard of care for a given clinical condition/situation

Guidelines

Tell you what to do

Clinical guidelines

- ✓ Evidence-based recommendations for broad clinical decision-making
- ✓ Issued by national/international organizations
- ✓ Advisory, not binding

VS

Protocol

Tells you how to do it

Clinical/medical protocol

- ✓ Institution-specific mandatory instructions for specific scenarios
- ✓ Ensures standardization, safety, and timely interventions
- ✓ Binding within the institution

Why do we need PBM protocols?*

In 2025, the WHO released comprehensive PBM guidance to improve global blood health, including:¹

Reducing complications associated with transfusions



Optimizing recovery by managing anemia and minimizing blood loss

Enhancing surgical safety

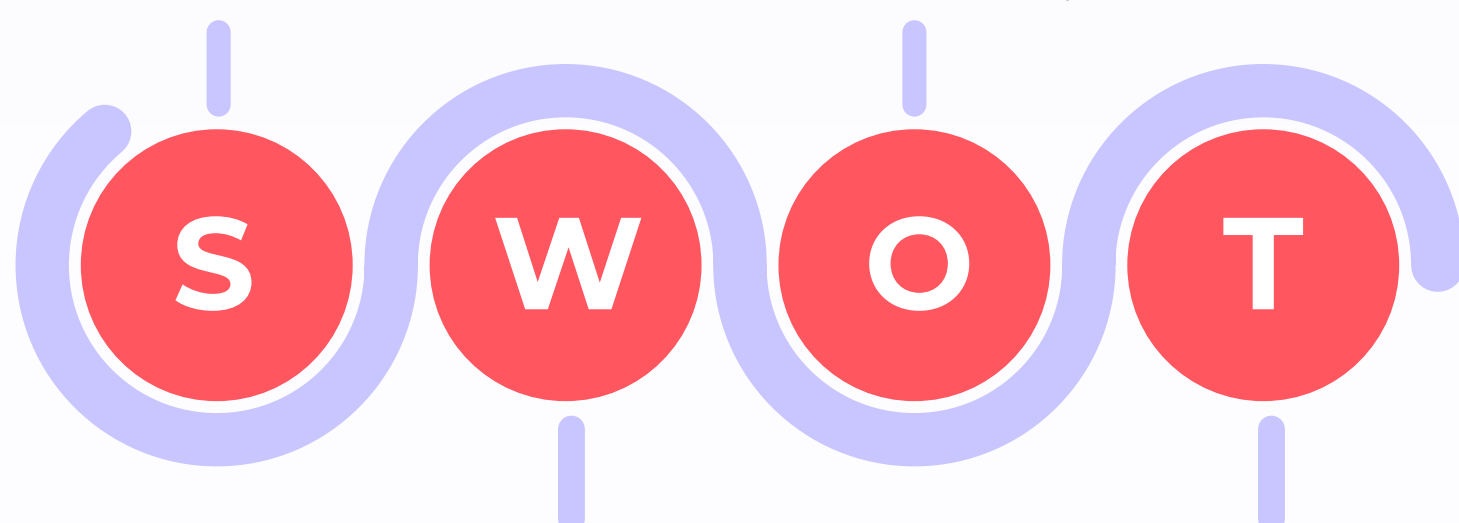


Strengths*

- Improves patient safety
- Reduces morbidity
- Cost effective

Opportunities*

- Introduction of new procedures leading to improved patient care
- Global health impact



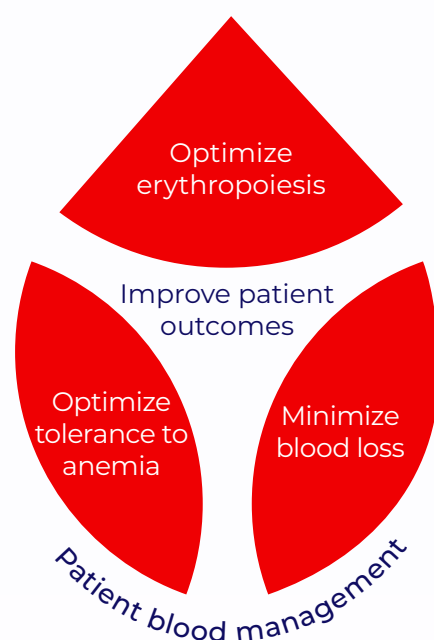
Weaknesses*

- Resource demands
- Requires training
- Complex implementation

Threats*

- Failure to reach interdisciplinary consensus
- The material produced will be too complicated
- Inadequate support/education and insufficient tools to motivate care providers to implement changes

The three-pillar matrix of perioperative PBM^{*2-4}



Preoperative:

- Screen and treat anemia (e.g., iron deficiency)
- Delay elective surgery if needed
- Communicate the problem with the patient

Intraoperative:

- Blood salvage
- Surgical techniques to reduce blood loss
- Coagulation support
- Antifibrinolytics (e.g., TXA)

Postoperative:

- Monitor and manage anemia
- Restrictive transfusion strategies

Examples of successful PBM initiatives⁵

1

Western Australia Department of Health state-wide PBM program



wapbm.org.au

2

The Nurse Ontario Transfusion Coordinators (ONTraC) program is a provincial PBM program in Canada (revised in 2020)



ONTraC program

3

Austrian institutional programs



Austrian Institute of Technology program information

PBM consensus statements

Muñoz 2017⁶ *International consensus statement on the peri-operative management of anaemia and iron deficiency*



Mueller 2019⁷ *Patient blood management: Recommendations from the 2018 Frankfurt Consensus Conference*



Quality control of PBM implementation

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PBM implementation

PBM is a patient-centered, systematic, evidence-based approach to improve patient outcomes by managing and preserving a patient's own blood while promoting patient safety and empowerment¹

Although PBM strategies are recommended by the WHO,² they remain underused across hospitals and institutions^{3–5}



Implementing PBM is challenging due to its multidisciplinary, multimodal nature and the need for organization-wide cultural change and collaboration among clinicians, managers, and regulators⁶

You can't improve it if you don't measure it!

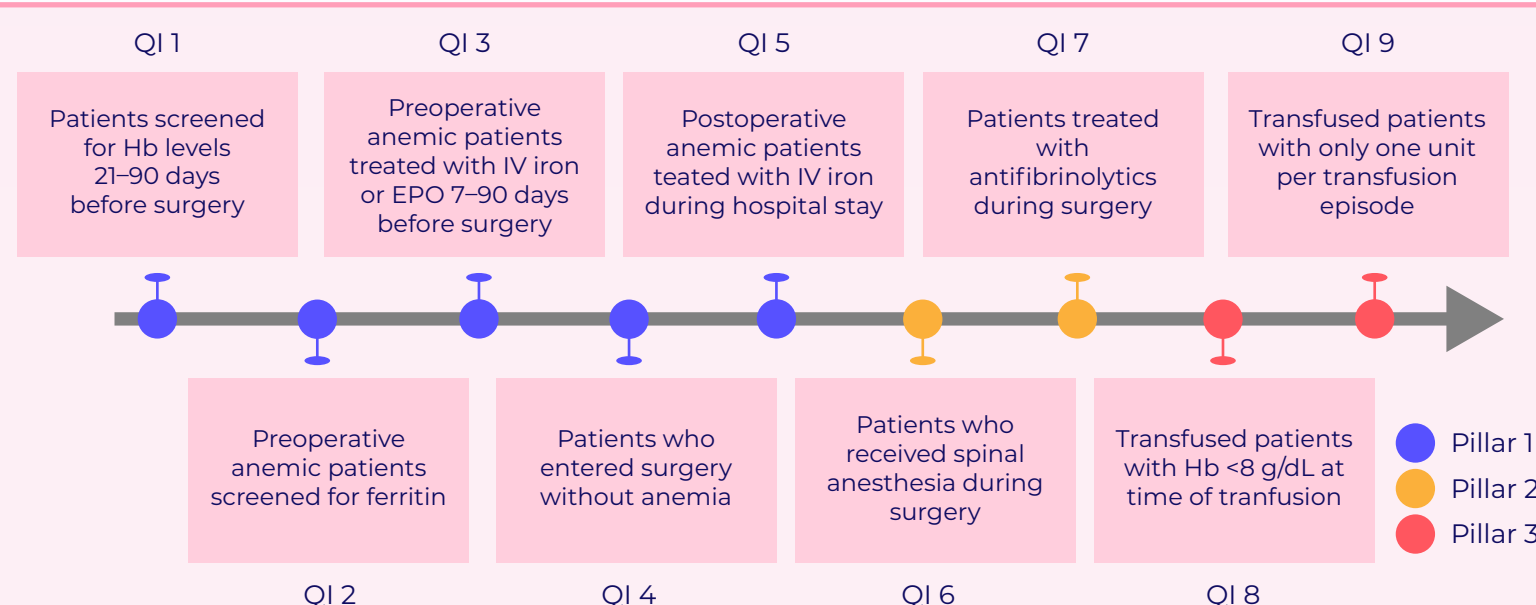
Current evidence on PBM's impact on clinical endpoints, adherence, and cost-effectiveness remains limited and requires further research⁷



Clinical recommendations and PBM best practices can be translated into a set of measurable KPIs⁶

The use of KPIs makes it easier for hospitals to measure and benchmark their PBM clinical programs and outcomes⁶

Perioperative PBM clinical pathway and quality indicators in a large hospital network in Spain⁵



Real-world example⁸

PBM implementation for hip and knee arthroplasty in 43 hospitals

- Retrospective analyses of association between adherence to PBM and outcome measures for the period 2016–2022
- N=30,926 patients
- Adherence to PBM was measured as a composite QI including nine individual QIs (QI 1–9)

Primary endpoint: 30-day postoperative complications

Secondary endpoints: Hospital LOS, number of patients transfused with RBCs, and units of RBCs transfused per patient

PBM adherence was associated with a reduced risk of:

30-day postoperative complications	Hospital LOS	Patients with RBC transfusions	RBC transfusions per patient
57%	23%	89%	51%

Applying **all eligible PBM interventions together is essential**, as missing one was associated with poorer outcomes



From guidelines to actions⁹

- Effective PBM improves surgical outcomes and reduces transfusion rates, complications, and healthcare costs
- PBM guidelines are well established, but real-world implementation is lacking. **The challenge is turning knowledge into clinical action**
- PBM requires system-level integration. It needs to be embedded into hospital systems with coordinated, multidisciplinary programs
- Dedicated leadership is essential
- Institutions should move toward **standardized, prioritized PBM protocols to reduce variation and improve outcomes**

POC testing for rapid diagnosis and targeted treatment in trauma: The role of coagulation factor concentrates

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Trauma-induced coagulopathy (TIC) refers to abnormal coagulation processes caused by traumatic injury¹



Early TIC is usually associated with hypocoagulability, linked to fibrinogen depletion and hyperfibrinolysis, which may result in uncontrolled hemorrhage



Late TIC is characterized by hypercoagulability, which may lead to TEEs and multiple organ failure

Approximately 25% of patients with severe injuries develop TIC; this is associated with a 35–50% mortality rate¹

Hypofibrinogenemia

During severe bleeding, **fibrinogen levels decrease to a critical value (<1.5–2 g/L) at an earlier stage** than other coagulation factors or platelets²



Point-of-care (POC) testing

Viscoelastic testing (e.g., ROTEM®), a POC test, provides **rapid, whole blood coagulation assessment**, including clot formation/strength and fibrinolysis³



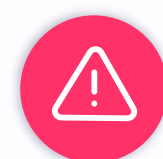
- A retrospective study investigating ROTEM® tests concluded that **FIBTEM A10/MCF provided early predictive information for massive transfusion** in trauma patients⁴
- Compared with standard coagulation tests, **use of viscoelastic testing to guide hemostatic resuscitation** in patients with severe injuries is associated with:⁵
 - **Increased proportion of patients alive and free of massive transfusion at 24 hours**
 - **Reduction in the use of blood products and related costs**



European trauma guidelines recommend early, repeated hemostatic monitoring and **goal-directed management**, with **viscoelastic testing** as a guiding option⁶

Use of CFCs versus FFP

- The RETIC study, a single-center, randomized trial, **compared first-line CFCs** (FC, 4F-PCC, and FXIII concentrate; n=50) **and FFP** (n=44) for the treatment of TIC⁷
- The study was terminated early due to a **high incidence of treatment failure** and **increased risk for massive transfusion in patients treated with FFP**, concluding that **first-line CFC is superior to FFP⁷**



Other studies have also demonstrated that **transfusion with FFP is associated with increased risk of negative clinical outcomes^{8–10}**

Use of TXA

Delayed treatment with TXA has been shown to **reduce its benefit¹¹**



In trauma patients with suspected TIC, no increase in survival with a favorable functional outcome at 6 months was observed with TXA vs placebo¹²



In trauma-associated bleeding, avoid massive transfusion by using goal-directed management targeted to individual patients' needs*

FXIII supplementation in surgical and traumatic bleeding

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A case-based perspective of postsurgical bleeding*



The patient:

- 69-year-old female
- Corpus uteri sarcoma
- Post-major debulking



History:

- Hyperinflammation
- Hepatorenal syndrome, kidney injury with stable renal function
- Liver function reduced, but LDH, AST, ALT, and bilirubin all normal



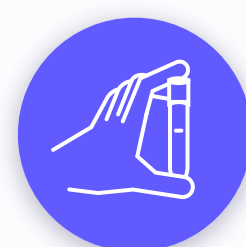
The challenge:

Diffuse bleeding 15 days postsurgery, with no causal event

Next diagnosis step?

Coagulation tests:

INR, aPTT, fibrinogen, and platelets **all normal**



Viscoelastic tests:

EX, FIB, and IN tests **all normal**

FXIII deficiency is easily missed¹



Signs of FXIII deficiency:[†]

- Diffuse, steady hemorrhage
- Hemorrhage occurs hours after a no-bleed interval
- Thromboelastography not sensitive enough to detect

FXIII deficiency: Background²



Congenital: Rare, sometimes severe, and caused by a wide variety of different mutations



Acquired: Caused by impaired synthesis (through hepatitis or acute liver failure), or increased consumption (in sepsis, trauma, leukemia, or major surgery)

FXIII levels: The full picture



Bleeding tendency does not always align with absolute FXIII activity level... **WHY?**[†]

FXIII activity <60% increases risk of bleeding complications⁶

A **significant postoperative decrease** in FXIII activity level can also be clinically relevant for bleeding tendency[†]

Clinical relevance of FXIII levels: Evidence from the literature

- Patients requiring **surgical reexploration** for bleeding show significantly **lower FXIII activity** than those who do not (59% vs 71%; $p=0.014$)³
- **FXIII deficiency** is associated with increased probability to receive **RBC transfusions** intraoperatively (OR=4.58; 95% CI: 3.46–6.05)⁴
- Patients with **lower FXIII** levels require **more pRBC transfusions** ($p<0.001$) and have significantly lower **Hb levels** ($p=0.0125$)⁵
- Patients with **sepsis** show a marked and sustained **reduction in FXIII activity** compared with both healthy individuals and surgical patients[‡]

Strategy for PBM postsurgery:



Exclusion diagnosis to **rule out other** causes of bleeding[†]



Perioperative monitoring of FXIII activity levels is recommended[†]



Substitute FXIII if clinical bleeding is present and FXIII activity <60%⁷



Suggested dose of FXIII at **20 IU/kg body weight per day⁷**

Benefits of viscoelastic testing for the management of postpartum hemorrhage

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PPH overview and challenges

PPH is defined as blood loss $\geq 1,000$ mL. It occurs in **1–10%** of deliveries and is a leading cause of maternal death in developing countries¹

Coagulopathy occurs in 23% of cases when blood loss is $\geq 1,500$ mL,² and the main causes include placental abruption, amniotic fluid embolism, and abnormal placentation³

Formula-driven transfusion strategies

risk unnecessary and harmful blood product use without addressing bleeding etiology³

VS

Goal-directed hemostasis

uses a targeted approach, leading to a reduction in transfusion of blood products²

Fibrinogen levels in PPH

1st

Fibrinogen is almost always the first, and frequently the only, coagulation factor to drop during PPH, and is a strong predictor of bleeding severity and associated comorbidities^{2–4}



Levels <2 g/L are linked to rapid progression to major obstetric hemorrhage, and very low fibrinogen can occur even with minimal blood loss (consumption coagulopathy)⁵



Monitoring fibrinogen helps guide timely and appropriate intervention⁵

Fibrinogen levels^{6,7}

Non-pregnant	At term	Immediate postpartum period
~2–4 g/L	~4–6 g/L	Up to ~8 g/L

Viscoelastic testing and its advantages

Viscoelastic tests provide rapid (initial results within 10 min), bedside, and reliable whole blood coagulation assessment, including clot formation, platelet contribution, and fibrinolysis^{8,9}



Coagulation management guided by viscoelastic testing:

- ✓ reduces blood product use^{10,11}
- ✓ improves perioperative outcomes^{2,12}
- ✓ is cost effective⁹

POC-guided protocols in obstetrics

POC-guided protocols identify patients needing fibrinogen supplementation and their use results in reduced transfusions and complications^{2,10–12}



Protocols **guide transfusion decisions** and **optimize coagulation management** by defining treatment thresholds based on ROTEM® parameters (e.g., FIBTEM A5, EXTEM CT), or TEG® parameters (e.g., alpha angle, MA)^{5,13}



It is important to confirm the parameter thresholds that trigger treatment

Studies have shown that **FIBTEM A5 <12 mm** correlates with severe bleeding and longer hospital stays, serving as an early biomarker for severe PPH^{3,5}

The equivalent **FIBTEM A5 value is ≤ 8 mm for ROTEM® Sigma cartridges** dated after April 2023¹⁴

The optimal TEG® cutoff values associated with predicting hypofibrinogenemia in PPH are **alpha angle <63 degrees and MA <60 mm**¹³

FIBTEM A5



Key recommendations for PPH management

- ✓ PPH management should avoid formula-driven transfusions due to risks of fibrinogen dilution³
- ✓ Goal-directed hemostasis, guided by viscoelastic testing, is an effective and efficient method of treating coagulopathy^{2,3}
- ✓ Fibrinogen levels are early predictors of severe hemorrhage⁵
- ✓ Etiology of PPH is crucial in diagnosing coagulopathy⁵
- ✓ Viscoelastic testing-guided management improves outcomes, reduces transfusions, and is cost effective^{2,9–12}

The role of FXIII concentrate in managing obstetric bleeding

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PPH is an increasingly common and important concern

The WHO definition of PPH is **blood loss ≥ 500 mL** within 24 hours postpartum¹

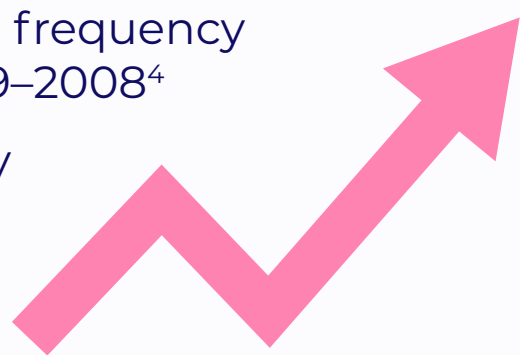
~30% of maternal deaths worldwide are hemorrhage related²



PPH is estimated to cause the death of a woman every 10 minutes³

The incidence of **PPH is increasing** and **postpartum blood loss is underreported**

- Severe PPH doubled in frequency in the US between 1999–2008⁴
- Undiagnosed PPH may be as common as diagnosed PPH⁵



Treatment recommendations for coagulopathy in PPH^{6–9}

To be carried out in parallel to surgical, mechanical, and supplementary measures

TXA: Early TXA administration immediately after PPH diagnosis

Procoagulant factors:

- The targeted administration of FXIII, platelet concentrates, or FC
- rFVIIa is reserved for severe PPH when uterotonics are insufficient

TXA and FC are *not* recommended for PPH prophylaxis



In the peripartum setting, FXIII is lost to a greater extent compared with fibrinogen, FII, and platelets,^{10,11} as such, FXIII may be a viable early treatment option¹²

FXIII has the highest susceptibility for depletion in the peripartal course

The **PPH-1300** study was a prospective study of >1,300 women undergoing standardized blood loss measurement within 36 hours before and after delivery, with measurements of **fibrinogen, FII and FXIII levels, Hb, and platelet count¹³**

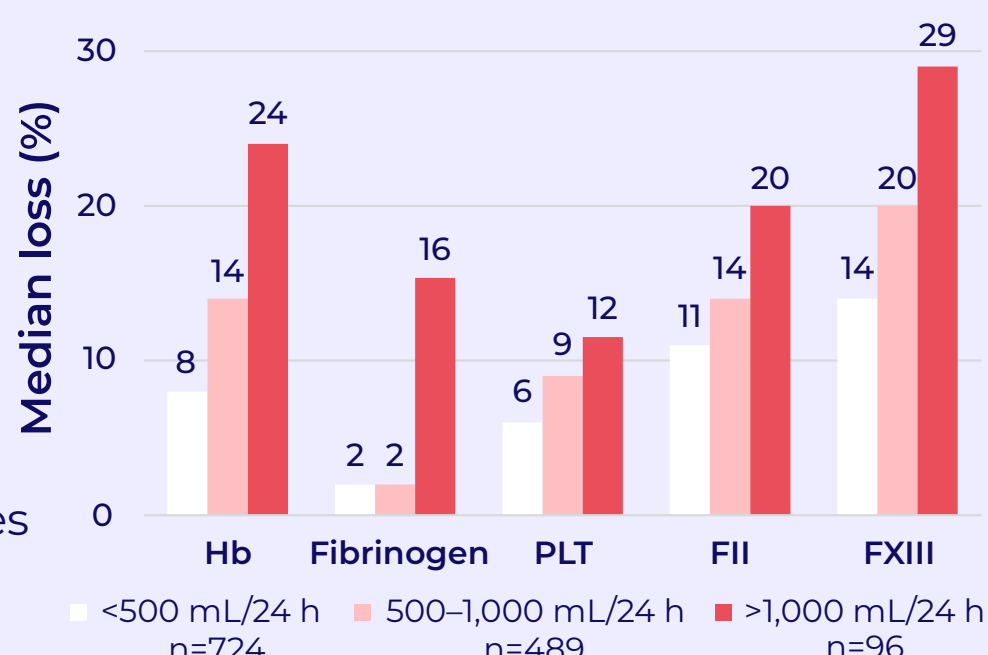


FXIII was the *only* parameter evaluated with a statistically significant impact on blood loss¹³

- A higher prepartum FXIII corresponded to lower postpartum blood loss, **irrespective of risk factors or delivery mode¹³**

These data indicate significantly different susceptibilities for loss and consumption of coagulation factors in the peripartum setting: **FXIII > FII > PLT > fibrinogen^{11,13}**

Median loss from pre- to postpartum values in Hb, PLT, and coagulation factors¹¹



In surgery, **FXIII deficiency** is associated with **poor patient outcomes:**^{14–17}



Increased bleeding



Increased blood product needs



Longer ICU stays

The role of thrombin generation and fibrinolysis in PPH¹⁸

The PPH-1300 study found that women who develop PPH *do not* have increased fibrinolytic activity or decreased thrombin generation prepartum; it is unlikely these are key prepartum factors that contribute to the **early** development of PPH

- Prepartum PAP complexes and prothrombin fragments are not different in women who do or do not develop PPH**

FXIII is a key modulator of postpartum blood loss



FXIII is the coagulation factor most susceptible to peripartum loss/consumption^{11,13}



Antifibrinolytics and increasing thrombin generation are unlikely to be an effective treatment **early on** in PPH¹⁸



FXIII is a prime candidate for an intervention trial for *early* therapy to improve outcomes in women with PPH¹²



PBM ESSENTIALS

MED-ALL-HCT-00209.
Date of preparation: October 2025



Some of the recommendations outlined in this document may not be applicable to the local indications for the available products. For country-specific information, please contact your local medical representative