

LA MEDICINA TRASFUSIONALE  
TRA EMOPATIE,  
EMOGLOBINOPATIE  
E BUON USO DEL SANGUE

Responsabile Scientifico dott. Francesco Bennardello

PROGRAMMA



Venerdì 08 marzo 2024

14:30-15:00 Saluti autorità e presentazione dell'evento formativo

PRIMA SESSIONE

Moderatori: Renato Messina - Francesco Bennardello

15:00-15:30 Nunzio Marletta - Il Patient Blood Management: una nuova opportunità

15:30-16:00 Daniele Aprile - La terapia trasfusionale: indicazioni mediche e chirurgiche

16:00-16:30 Nuccio Zisa - La sicurezza della trasfusione: come prevenire l'errore trasfusionale

16:30-17:00 Discussione

17:00-17:30 Pausa

SECONDA SESSIONE

Moderatori: Nunzio Marletta - Santi Sciacca

17:30-18:00 Elisa Cannizzo - Le anemie: fisiopatologia e classificazione

18:00-18:30 Luisa Ferraro - Il trattamento delle anemie e la somministrazione del ferro per via endovenosa

18:30-19:00 Pietro Trovato - La gestione clinica dei Testimoni di Geova: un approccio collaborativo

19:00-19:30 Discussione

Sabato 09 marzo 2024

TERZA SESSIONE

Moderatori: Pietro Bonomo - Carmelo Fidone

09:00-09:30 Vincenzo Spadola - L'eritroexchange nella terapia della drepanocitosi

09:30-10:00 Carlo Rapisarda - La gestione delle talassemie: approccio multidisciplinare

10:00-10:30 Francesco Bennardello - La prevenzione della MEN da anticorpi anti Rh-D

10:30-11:00 Discussione

11:00-11:30 Pausa

QUARTA SESSIONE

Moderatori: Sergio Cabibbo - Francesco Bennardello

11:30-11:50 Agostino Antolino - Poliglobulia e policitemia

11:50-12:10 Giovanna Oriella Manenti - Le trombocitemie

12:10-12:30 Giovanni Digiacomo - Trombocitemia e policitemia: il ruolo del medico curante

12:30-12:50 Massimo Poidomani - Le coagulopatie: emorragia e trombofilia

12:50-13:10 Giovanna Fretto - La diagnostica di laboratorio delle coagulopatie

13:10-13:30 Discussione

13:30-14:00 Compilazione dei questionari di apprendimento e di gradimento

con il patrocinio di:



con il contributo  
non condizionante di:



# Il Patient Blood Management: una nuova opportunità

## Dr. Nunzio Angelo Marletta SIMT ASP di Caltanissetta

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Il sottoscritto, in qualità di Relatore  
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nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatore di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

# Global prevalence of anaemia, blood loss and bleeding disorders and their etiologies



World Health  
Organization

## 2.9+ BILLION

individuals with anaemia (2-4,195)  
and/or micronutrient deficiencies (4-7)

- Iron deficiency and other micronutrient deficiencies
- Pre-operative anaemia in surgical patients (IDA, AI)
- Anaemia following surgical interventions
- Anaemia in patients with common noncommunicable diseases
- Anaemia in patients with oncological and haematological malignancies
- Anaemia in patients with infectious diseases (including viral and parasitic infections)
- Hospital-acquired anaemia in patients without haemorrhage or surgery

## 600+ MILLION

Individuals with chronic or acute  
blood loss and/or bleeding disorders (32-44)

- Major surgery
- Medical and surgical ICU
- Obstetric/peripartum bleeding
- Heavy menstrual bleeding
- Gastrointestinal bleeding
- Haemoglobinopathies
- Coagulopathies
- Phlebotomy/venipunctures
- Trauma

# Meta-analysis of the association between preoperative anaemia and mortality after surgery

- **949'449 patients of 24 studies analyzed**
- **39% of patients were anemic (WHO definition)**
- **Anemia was associated with**
  - ⇒ Perioperative mortality ↑ - OR 2.90 (2.30 – 3.68,  $p < 0.001$ )
  - ⇒ Acute kidney injury ↑ - OR 3.75 (2.95 – 4.76,  $p < 0.001$ )
  - ⇒ Infections ↑ - OR 1.93 (1.06 – 1.55,  $p < 0.01$ )
  - ⇒ Stroke in cardiac surgery ↑ - OR 1.28 (1.17 – 3.18,  $p < 0.01$ )
  - ⇒ RBC transfusion ↑ - OR 5.04 (4.12 – 6.17,  $p < 0.001$ )

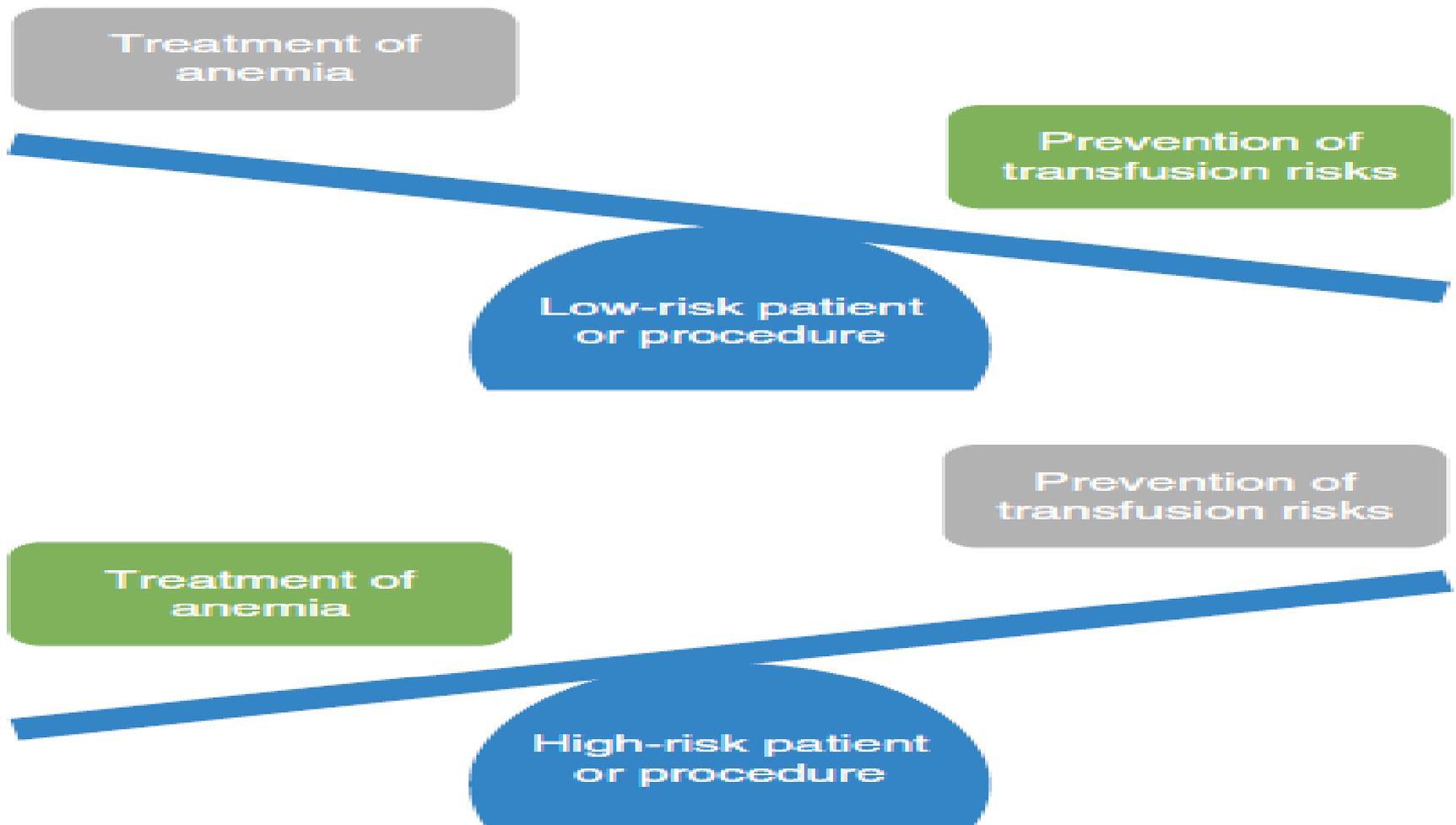
Does transfusion<sup>y</sup> do what it is intended to do—improve outcome or prevent adverse outcomes?

- There are few if any articles that support transfusion actually improving patient outcomes.
- The majority of database papers show associations between transfusion utilization and with immunosuppression, increased infection, increased renal failure, multisystem organ failure, and death.

## Studies reporting a dose-response increase in adverse outcomes associated with red blood cell transfusion

| Author/Year                    | Population      | Sample size | Dose-response increased adverse outcome   |
|--------------------------------|-----------------|-------------|---|
| Shaw 2014 <sup>19</sup>        | Cardiac surgery | 3'516       | Mortality   |
| Horvarth 2013 <sup>20</sup>    | Cardiac surgery | 5'158       | Infection   |
| Mikkola 2012 <sup>21</sup>     | Cardiac surgery | 2'226       | Stroke  |
| Stone 2012 <sup>22</sup>       | Cardiac surgery | 1'491       | Mortality   |
| Van Straten 2010 <sup>23</sup> | Cardiac surgery | 10'425      | Mortality   |
| Hajjar 2010 <sup>24</sup>      | Cardiac surgery | 512         | Morbidity & mortality   |
| Karkouti 2009 <sup>25</sup>    | Cardiac surgery | 3'460       | Acute kidney injury   |
| Scott 2008 <sup>26</sup>       | Cardiac surgery | 1'746       | Postoperative LOS   |
| Murphy 2007 <sup>27</sup>      | Cardiac surgery | 8'500       | Infection & ischemic events   |
| Kulier 2007 <sup>28</sup>      | Cardiac surgery | 5'065       | Cardiac and non-cardiac adverse events  |
| Banbury 2006 <sup>29</sup>     | Cardiac surgery | 15'592      | Septicemia, bacteremia, superficial & deep sternal wound infection  |
| Koch 2006 <sup>30</sup>        | Cardiac surgery | 11'963      | In-hospital mortality, renal failure, postoperative ventilatory support, postoperative infection, cardiac and neurologic morbidity, overall postoperative morbidity |
| Koch 2006 <sup>31</sup>        | Cardiac surgery | 10'289      | Long-term (10-years) survival   |
| Koch 2006 <sup>32</sup>        | Cardiac surgery | 7'321       | Functional recovery   |
| Rogers 2006 <sup>33</sup>      | Cardiac surgery | 9'218       | Infection   |
| Chelemer 2002 <sup>34</sup>    | Cardiac surgery | 533         | Bacterial infection   |
| Leal-Noval 2001 <sup>35</sup>  | Cardiac surgery | 738         | Infection, pneumonia  |

*Adapted from Farmer SL, Hofmann A, Isbister J. Transfusion and Outcomes. Patient Blood Management 2<sup>nd</sup> Edition Thieme; Stuttgart, New York: 2015*



La decisione di effettuare una trasfusione **dipende dalle condizioni del paziente e dall'invasività della procedura**. Nei pazienti relativamente sani e/o nelle procedure a basso rischio, l'equilibrio si orienta verso soglie restrittive per le trasfusioni (pannello superiore), mentre nei casi di pazienti ad alto rischio e/o procedure a rischio elevato, l'anemia viene trattata a rischio di complicanze legate alla trasfusione (pannello inferiore).

# Cost-Effectiveness Analysis: What It Really Means for Transfusion Medicine Decision Making

*Transfusion Medicine Reviews*, Vol 23, No 1 (January), 2009: pp 1-12

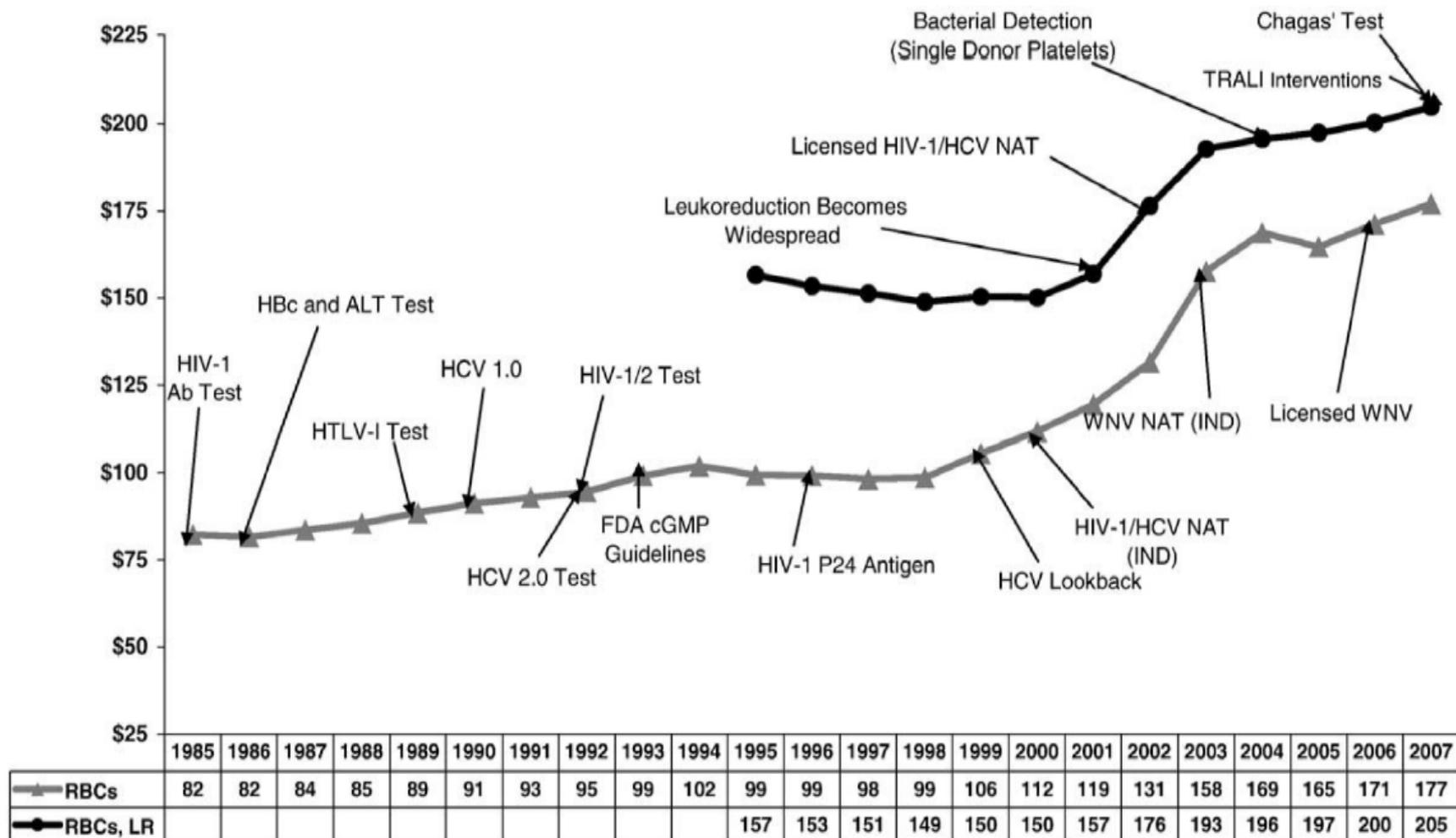
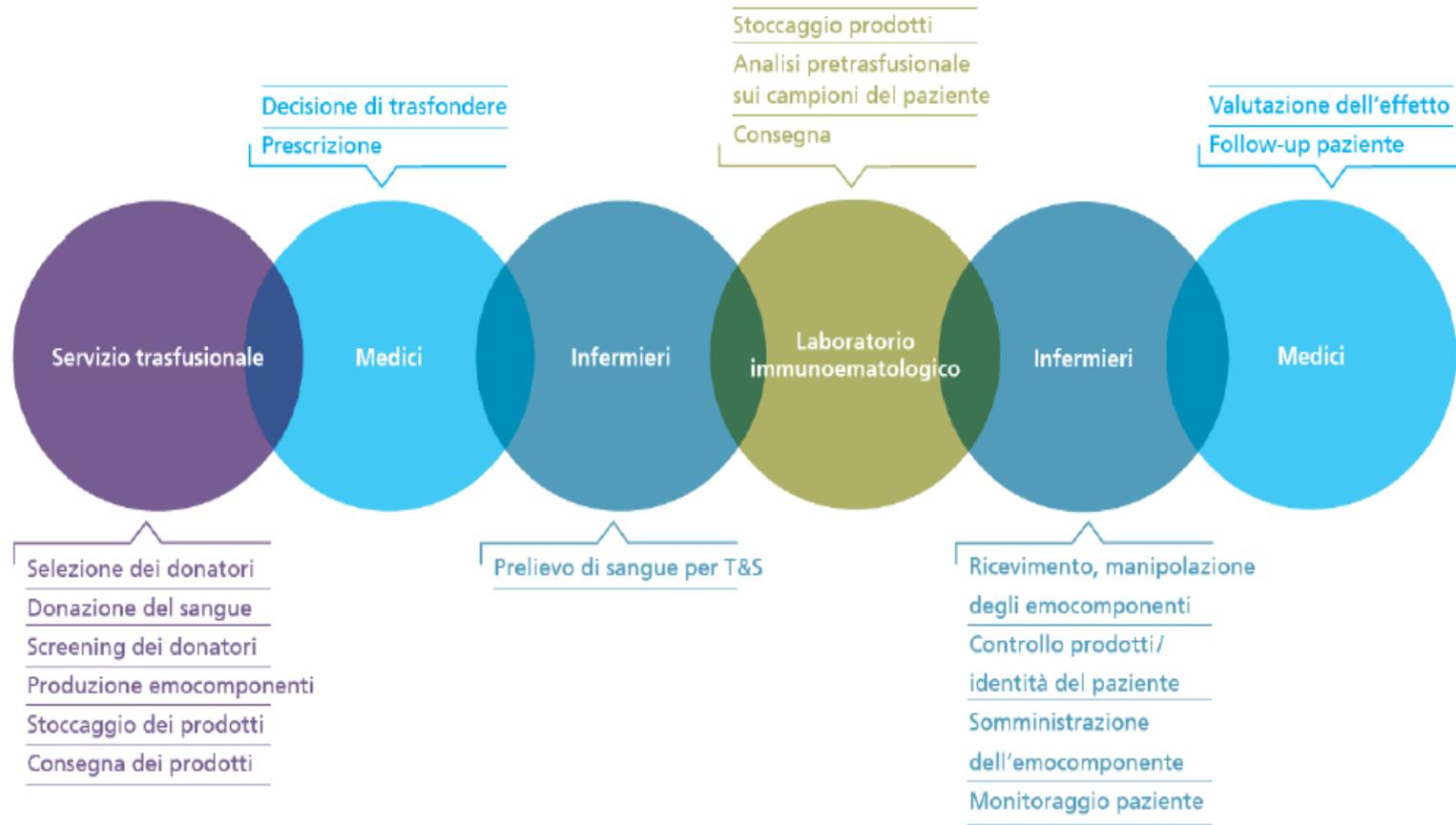


Fig 1. Average per unit red blood cell charge to hospitals by America's Blood Centers members in the last 20 years with the date of implementation of the additional safety measures indicated, adjusted to 2007 US dollars. The gray line represents nonleukoreduced red blood cells and the black line represents leukoreduced red blood cells. Permission to use granted by America's Blood Centers,

# Valutazione dei costi trasfusionali in un approccio PBM-based



## FASI DEL PROCESSO TRASFUSIONALE

## Blood: Fiend or/and Foe? | INCE vs. SHANDER

*Blood is crucial for life. The “holy” equation of oxygen delivery (DO<sub>2</sub>) explains us that blood (in this term: hemoglobin) is one of the three main components of “vitality”. So why should I stop myself of increasing the Hb, and maximise the DO<sub>2</sub> in this way? ..... a lot of things.*

*There are numerous “guidelines” and “recommendations” about the rules of blood transfusion. Almost none of them work well: The blood transfusion is still a matter of “instinct”, even in developed countries. Now we have the “Patient Blood Management”: What is its difference to other “guidelines”?*

*Maybe the clinician should make a calculation /estimation before “each and every” transfusion whether this would lead to an increase in oxygenation, instead of following the guidelines. But is this feasible?*

*Aryeh Shander is the Godfather of “Patient Blood Management”; and Can Ince is “the” researcher of tissue oxygenation.*

**Nüzhet Mert Şentürk**  
Editor

## The Yin and Yang of Blood Transfusion

**Aryeh Shander, Tamara Friedman**

*Department of Anesthesiology and Critical Care Medicine, Englewood Hospital and Medical Center, Team Health Research Institute, Englewood, NJ, USA*

Few physicians will argue against the statement that blood transfusions carry certain risks. There is also little debate over the fact that they can benefit those with hemorrhage or non-functioning bone marrow. Most of the salient debate in the literature centers on the benefits/risk ratio of blood component therapy. Besieged with repeated studies on restrictive vs. liberal transfusion, the clinician is left with only one treatment modality for the patient. By centering on transfusion, other more effective or less risk-associated therapies are ignored. This is problematic, as transfusions may prove to be associated with risks higher than that posed by the anemia, especially if there is no clinical or physiological concern (1). The quest for safe and effective blood transfusions is the opposing debate, and that side of the argument has no place in the treatment of anemia in majority of hospitalized and non-hospitalized patients with anemia.

Perhaps, the problem is that the debate over transfusions is presented in such a dichotomous manner. In truth, both blood transfusions and anemia carry significant risks, and they are both associated with increased morbidity and mortality (2). Instead of quibbling over which risk is greater, physicians need to move toward finding the best solution for individual patients, as the symp-

# *PATIENT BLOOD MANAGEMENT*

## 1st Pillar

Diagnose  
and  
manage  
Anaemia

## 2nd Pillar

Minimise  
blood loss  
-  
Control  
bleeding

## 3rd Pillar

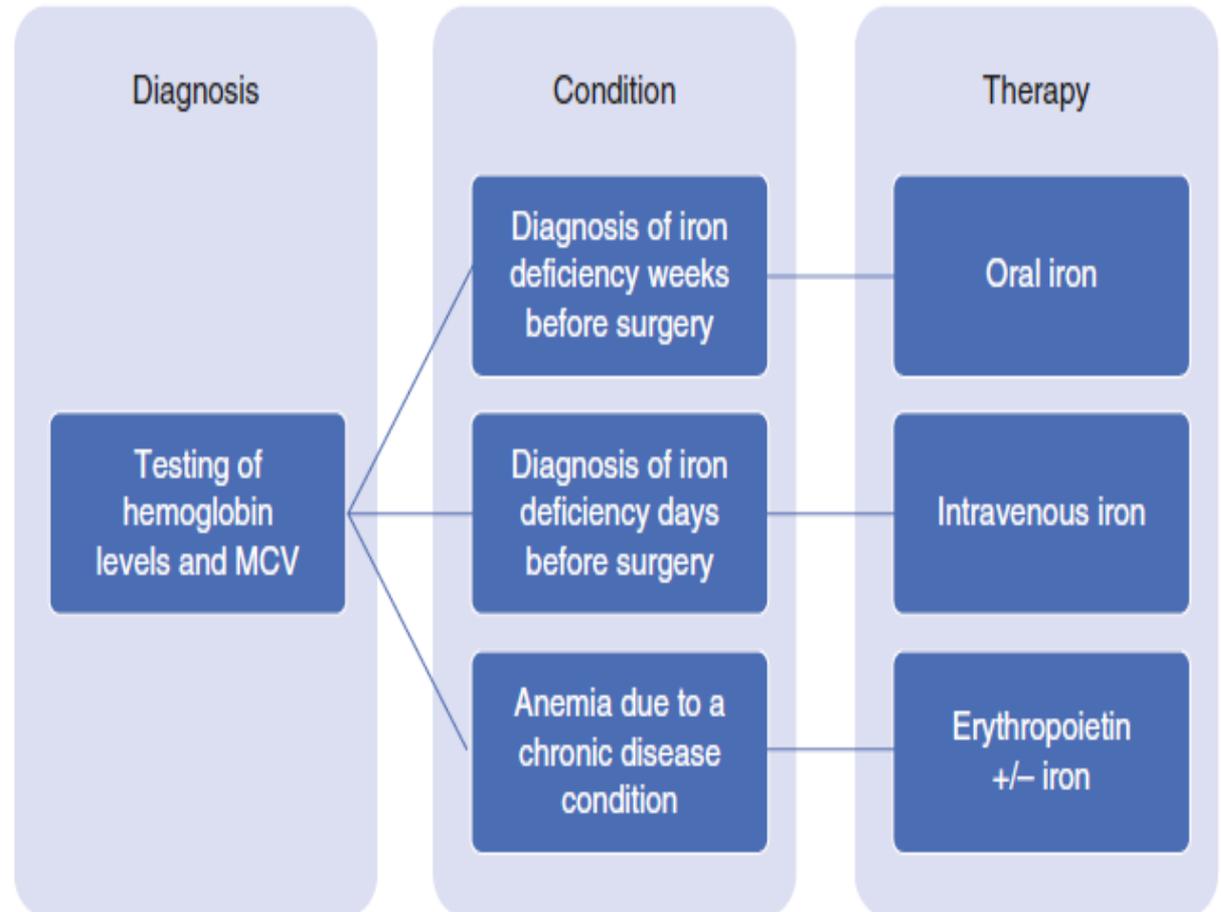
Avoid  
unnecessary  
transfusion

**Multidisciplinary team approach**

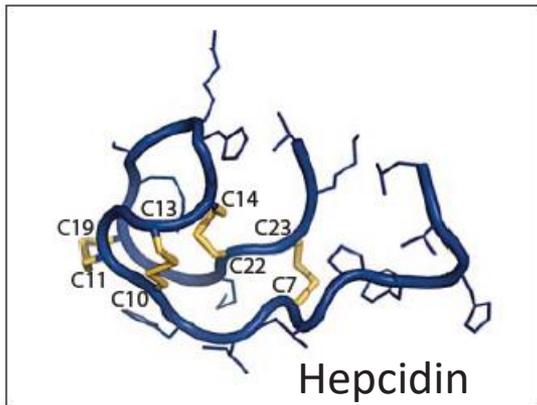
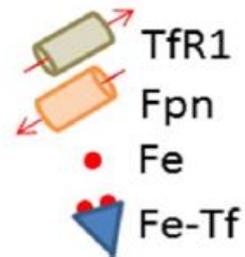
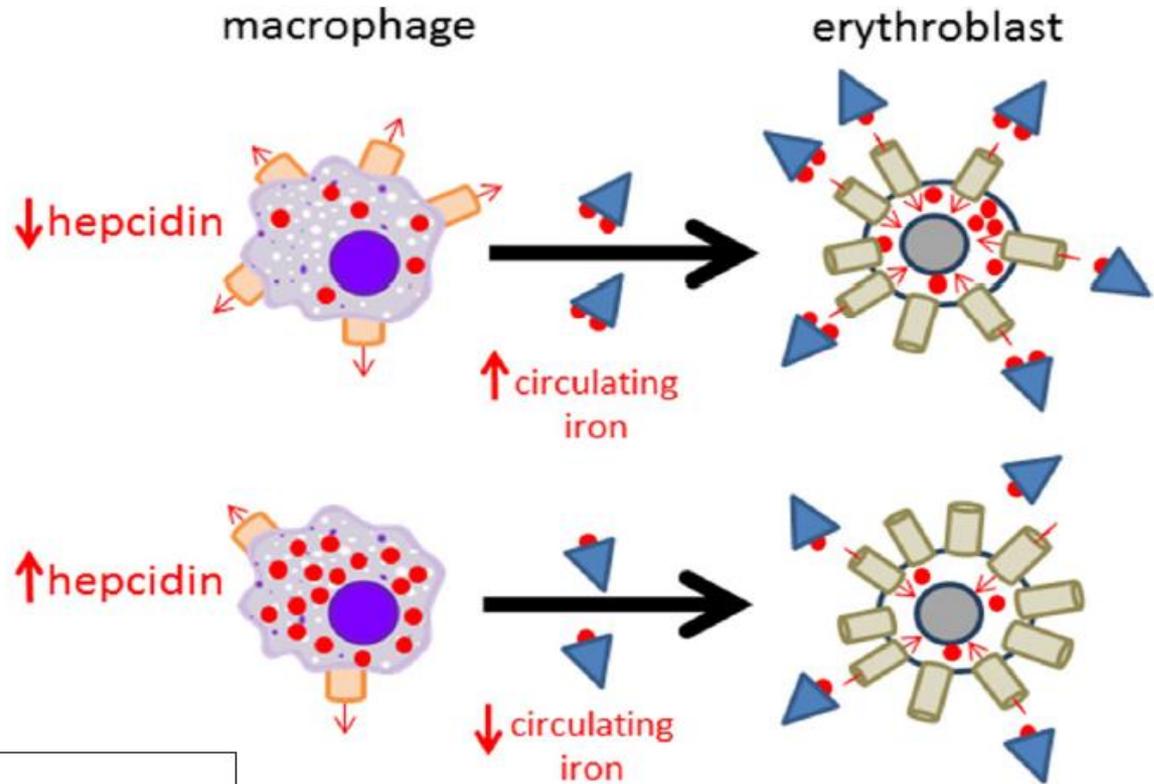
# PATIENT BLOOD MANAGEMENT

## 1st Pillar

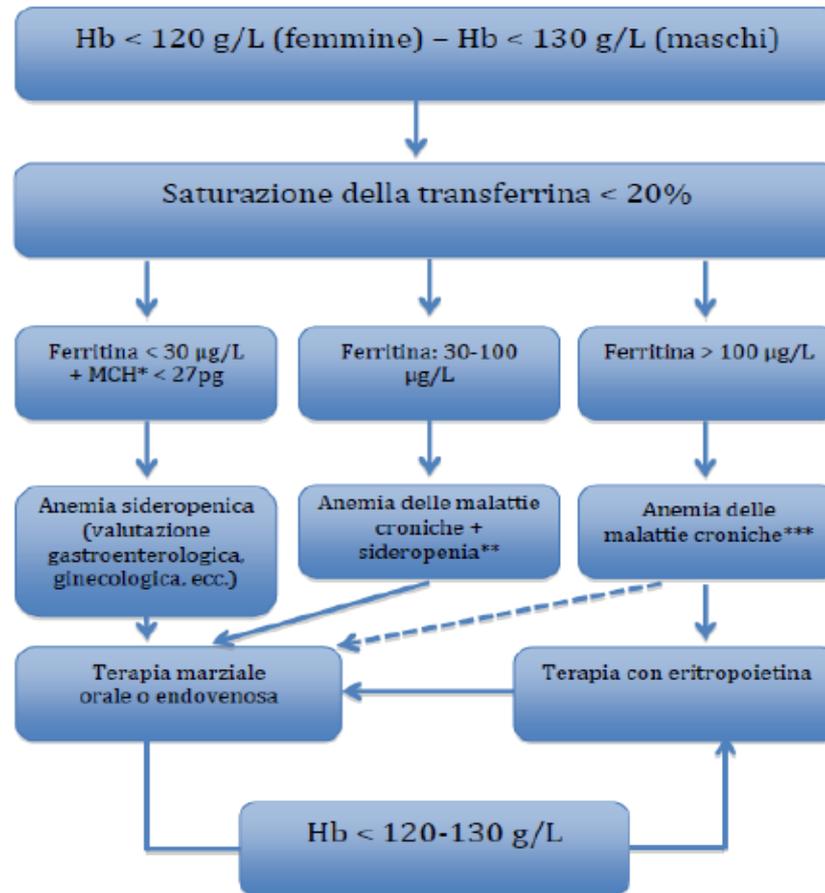
Diagnose  
and  
manage  
Anaemia



# Hepcidin-ferroportin axis in health and disease



# PBM: Algoritmo per la diagnosi di anemia sideropenica



# PBM: Classificazione degli interventi chirurgici in elezione in base al rischio emorragico.

## **Interventi con rischio emorragico clinicamente non importante**

- interventi di odontoiatria
  - estrazioni di 1 o 3 denti
  - chirurgia paradontale
  - incisione di ascesso
  - posizionamento di impianto
- interventi di oculistica
  - cataratta o glaucoma
- endoscopia senza chirurgia
  - chirurgia superficiale
  - incisione di ascessi
  - piccole escissioni dermatologiche

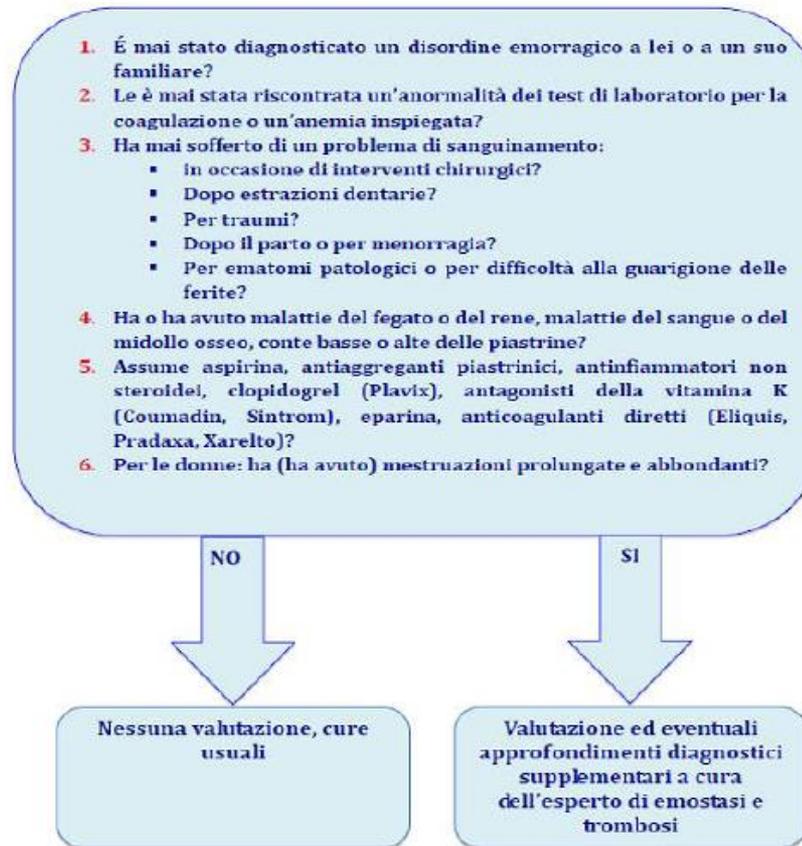
## **Interventi a basso rischio emorragico**

- endoscopia con biopsia
- biopsia della prostata o della vescica
- ablazione per tachicardia sopra-ventricolare (inclusa singola puntura trans-settale sinistra)

## **Interventi ad alto rischio emorragico**

- ablazione complessa
- anestesia spinale o epidurale; puntura lombare
- chirurgia toracica
- chirurgia addominale
- **chirurgia ortopedica maggiore**
- biopsia epatica
- resezione transuretrale della prostata
- biopsia renale

# PBM: Valutazione iniziale dei disordini emorragici



# 1° PILASTRO



- ANEMIA CLINIC (CONSULENZA PREOPERATORIA, CARTELLA CLINICA CONDIVISA, CONSULENZA CHIRURGICA PREOPERATORIA).



- DIAGNOSI E TRATTAMENTO ANEMIA PREOPERATORIA (PDTA)



- STUDIO DIATESI EMORRAGICA-TROMBOTICA

# PATIENT BLOOD MANAGEMENT

## 2nd Pillar

**Minimise  
blood loss  
-  
Control  
bleeding**



# Patient blood management using dedicated personnel in the operating room—you get what you pay for

Richard R. Gammon 



OneBlood, Scientific, Medical, Technical  
Direction, Orlando, Florida, USA

## Correspondence

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Commodity Circle, Orlando, FL 32819, USA.  
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## Summary

A patient blood management (PBM) strategy can be applied to the process of intraoperative cell salvage for re-infusion during surgery. Stoneham et al. describe an effective PBM strategy applied to abdominal aortic aneurysm repair and emphasise the importance of a qualified and experienced intraoperative cell salvage practitioner to improve the safety and effectiveness of the approach.

Commentary on: Stoneham et al. Intraoperative cell salvage using swab wash and serial thromboelastography in elective abdominal aortic aneurysm surgery involving massive blood loss. *Br J Haematol* 2022 (Online ahead of print). doi: 10.1111/bjh.18523.

## KEYWORDS

antifibrinolytic therapy, patient blood management, thromboelastography

# Procoagulant therapies

Coagulation factor deficiency

Fibrinogen concentrate

Cryoprecipitate

Factor XIII

Thrombin generation

Prothrombin Complex Concentrate (PCC)

Recombinant factor VIIa (rFVIIa)

Antifibrinolytic therapy

Tranexamic acid

$\epsilon$ -aminocaproic acid

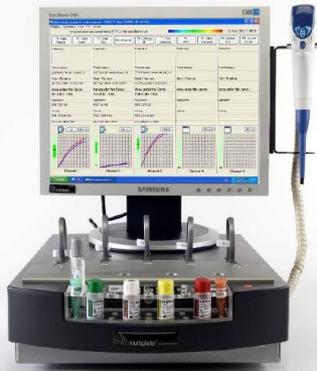
Aprotinin

Platelet dysfunction

Desmopressin

# USO DEI POINT OF CARE

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Comprehensive platelet diagnostics



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# 2° PILASTRO



- Costituzione di un gruppo dedicato formato da Tecnici/Infermieri perfusionisti



- Implementazione delle strategie di contenimento delle perdite perioperatorie (antifibrinolitici, colla di fibrina, ecc...)



- Monitoraggio emostatico-coagulativo (creazione di algoritmi decisionali terapeutici condivisi, uso dei POC)

# PATIENT BLOOD MANAGEMENT

**3rd Pillar**

**Avoid  
unnecessary  
transfusion**

COMMENTARY

## Are We Transfusing Too Much Blood?

George D. Lundberg, MD

January 30, 2023



George D. Lundberg, MD

Would you be surprised if I said that nearly half of all blood transfusions administered in hospitals in the United States between 2012 and 2018 were unnecessary?

# This guidance is based on the National Blood Transfusion Committee (NBTC)

## Indication Codes for Transfusion (January 2020)

The indications for transfusion provided below are taken from national guidelines for the use of blood components in adults (see references). Amalgamation into this summary document aims to act as a prompt for clinicians to facilitate appropriate use and to enable robust documentation of indications. Each indication has been assigned a number, to permit reproducible coding, when requesting blood or for documentation purposes. Specific details regarding the patient's diagnosis and any relevant procedures to be undertaken should also be provided at request either on a written request form, electronic blood order or by telephone when the request is urgent. These are current guidelines and may change depending on new evidence.

### Red cell concentrates

Dose: in the absence of active bleeding, use the minimum number of units required to achieve a target Hb. Assume an increment of 10g/L per unit for an average adult.

#### R1. Acute bleeding

Acute blood loss with haemodynamic instability. After normovolaemia has been achieved/ maintained, frequent measurement of Hb (including by near patient testing) should be used to guide the use of red cell transfusion. Suggested thresholds below



#### R2. Hb ≤ 70g/L stable patient

Acute anaemia. Consider an Hb threshold of 70g/L. Target Hb of 70-90g/L to guide red cell transfusion. Different recommendations (based on weak evidence) from other organisations e.g. Association of Anaesthetists

#### R3. Hb ≤ 80g/L stable patient and acute coronary syndrome

Use an Hb threshold of 80g/L and a target Hb of 80-100g/L

#### R4. Chronic transfusion dependent anaemia

Transfuse to maintain an Hb which prevents symptoms. Suggest an Hb threshold of 80g/L initially and adjust as required. Haemoglobinopathy patients require individualised Hb thresholds depending on age and diagnosis

#### R5. Radiotherapy maintain Hb ≥ 100g/L

There is some evidence for maintaining an Hb of 100g/L in patients receiving radiotherapy for cervical, and possibly other tumours

#### R6. Exchange transfusion

### Fresh frozen plasma (FFP)

Dose: 15-20ml/kg body weight, often equivalent to 4 units in adults.

#### F1. Major haemorrhage

In the trauma setting transfuse empirically in a 1:1 ratio with red cells. Other settings give FFP in at least a 1 unit:2 unit ratio with red cells until results from coagulation monitoring are available. Once bleeding is controlled, further FFP should be



and APTT (keep PT/APTT ratio of 1.5:2.0). Use of viscoelastic haemostatic

without major haemorrhage. FFP required if coagulopathy. PT > 1.5, or local protocol range for near-patient viscoelastic

#### Pre-procedure

Prophylactic use when coagulation results are abnormal e.g. disseminated intravascular coagulation and invasive procedure is planned

#### F4. Liver disease with PT Ratio/INR >2 and pre-procedure

FFP not usually required before invasive procedure if PT ratio/INR is <2 and if there is no significant risk of bleeding

#### F5. TTP/plasma exchange

#### F6. Replacement of single coagulation factor

# Better Blood Transfusion (BBT)

# This guidance is based on the National Blood Transfusion Committee (NBTC)

## Indication Codes for Transfusion (January 2020)

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### Prothrombin complex concentrate

Dose should be determined by the situation and INR. Local guidelines should be followed.

**PCC1. Emergency reversal of VKA for severe bleeding** or head injury with suspected intracerebral haemorrhage.

**PCC2. Emergency reversal of VKA pre emergency surgery**

### Cryoprecipitate

Dose: 2 pooled units, equivalent to 10 individual units, will increase fibrinogen in an average-sized adult. Cryoprecipitate should be used with FFP wherever there is a requirement for volume, except in the rare setting of isolated deficiency of fibrinogen.

- C1. Clinically significant bleeding and fibrinogen <1.5g/L (<2g/L in obstetric bleeding)**
- C2. Fibrinogen <1g/L and pre procedure, with a risk of bleeding**
- C3. Bleeding associated with thrombolytic therapy**
- C4. Inherited hypofibrinogenaemia, fibrinogen concentrate not available**



### Platelet concentrates

Dose: for prophylaxis, do not routinely transfuse more than 1 adult therapeutic dose. Prior to invasive procedure or to treat bleeding, consider the size of the patient, previous increments, and the target count.

#### Prophylactic platelet transfusion

- P1. Plt <10 x 10<sup>9</sup>/L reversible bone marrow failure**  
Not indicated in chronic bone marrow failure if not on intensive treatment, and not bleeding
- P2. Plt 10 – 20 x 10<sup>9</sup>/L sepsis/haemostatic abnormality or other additional risk factor for bleeding**

#### Prior to invasive procedure or surgery

- P3. To prevent bleeding associated with invasive procedures**
    - P3a Plt ≤20 x 10<sup>9</sup>/L - central venous line
    - P3b Plt ≤40 x 10<sup>9</sup>/L - pre lumbar puncture/spinal anaesthesia
    - P3c Plt ≤50 x 10<sup>9</sup>/L - pre-percutaneous liver biopsy/major surgery
    - P3d Plt ≤80 x 10<sup>9</sup>/L - epidural anaesthesia
    - P3e Plt ≤100 x 10<sup>9</sup>/L - pre critical site surgery e.g. CNS/Eye
- Transfusion prior to bone marrow biopsy is not required



#### Therapeutic use to treat bleeding (WHO bleeding grade 2 or above)

- P4a Plt <50 x 10<sup>9</sup>/L - Major haemorrhage**
- P4b Empirically in a Major Haemorrhage Pack / Protocol**
- P4c Plt <100 x 10<sup>9</sup>/L - Critical site bleeding e.g. CNS**
- P4d Plt <30 x 10<sup>9</sup>/L - Clinically significant bleeding**

#### Specific clinical conditions

- P5a DIC pre procedure or if bleeding**
- P5b Primary Immune thrombocytopenia (emergency treatment pre-procedure/severe bleeding)**

#### Platelet dysfunction

- P6a Consider if critical bleeding on anti-platelet medication**
- P6b Inherited platelet disorders directed by specialist in haemostasis**



**ONLY**  
**ONE**

**UNA** TRASFUSIONE  
**UNA** DECISIONE CLINICA  
INDIPENDENTE

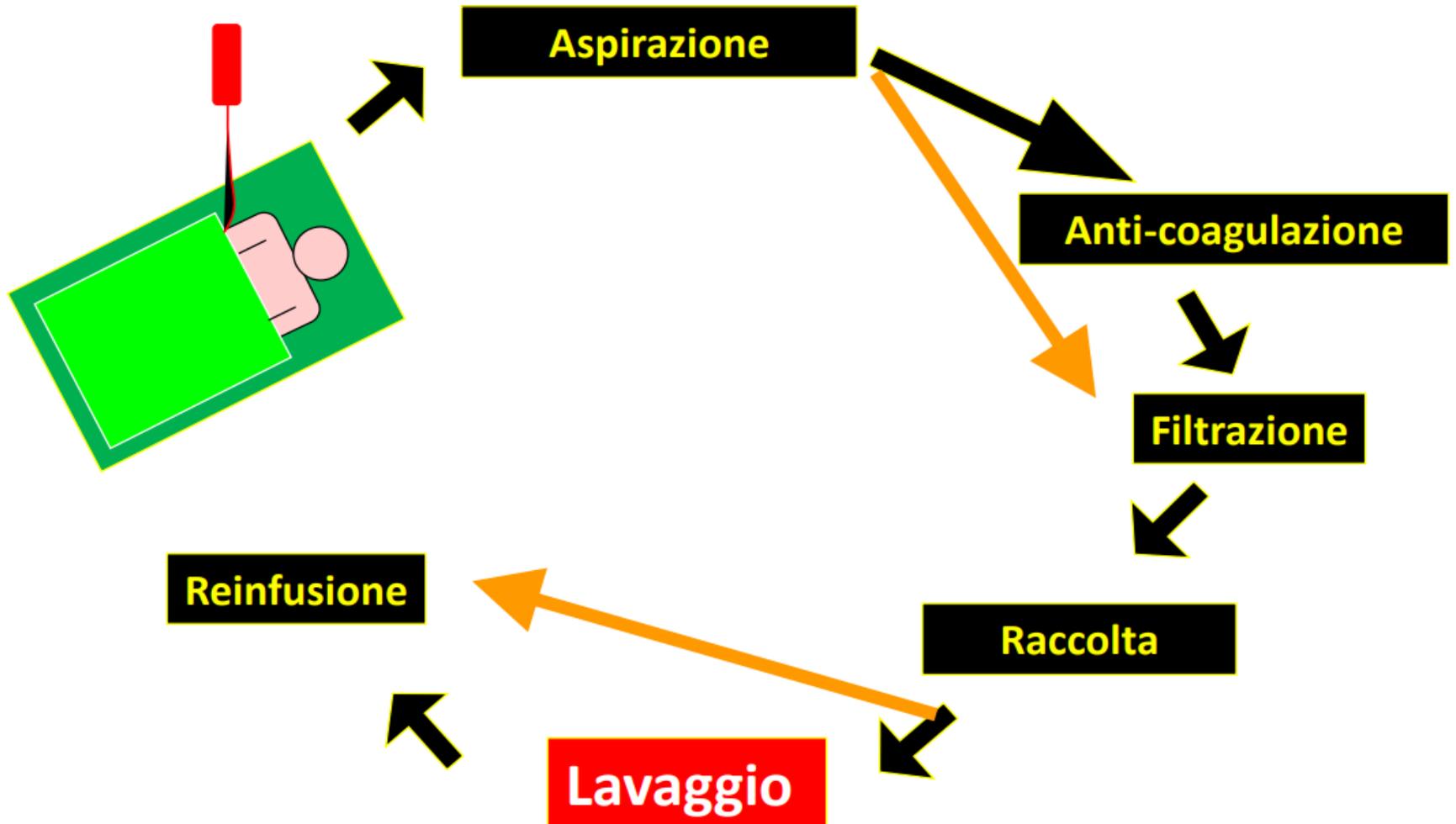


# Anemia post-operatoria: monitoraggio

- La flessione dei valori di Hb viene tendenzialmente attribuita a due fattori
  1. Le perdite ematiche perioperatorie
  2. Un'inadeguata somministrazioni di liquidi
- Frequenti prelievi ematici per gli esami di laboratorio
- Sanguinamenti gastrointestinali legati allo stress
- Effetti avversi a farmaci somministrati

# Recupero Perioperatorio

## Intraoperatorio e/o Postoperatorio



# TERAPIA DI SUPPORTO CON FERRO

- FERROGLUCONATO
- FERROCARBOSSIMALTOSIO
- ERITROPOIETINA

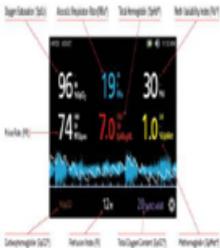
# 3° PILASTRO



- ATTIVAZIONE E COORDINAMENTO DEL RECUPERO POST OPERATORIO

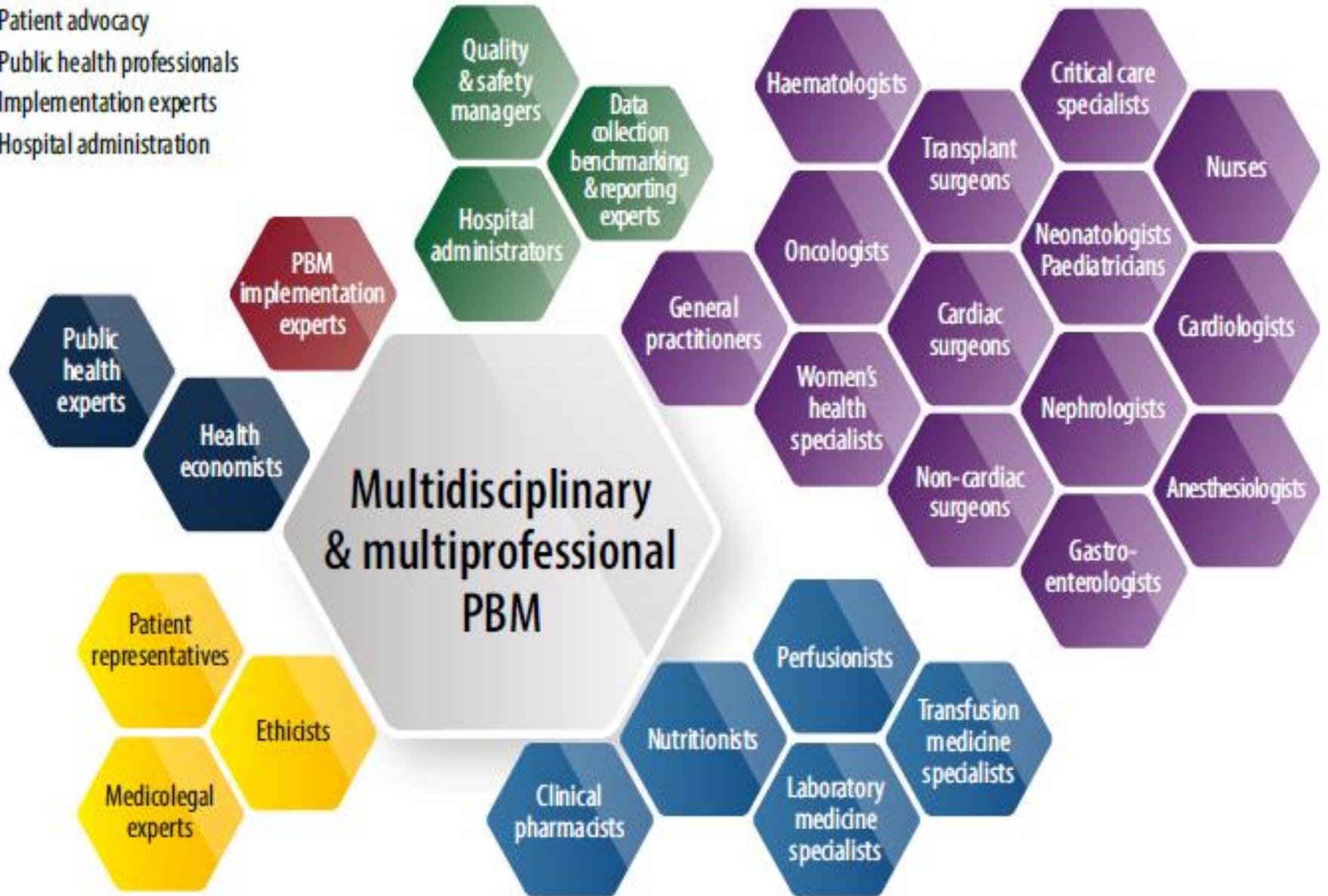


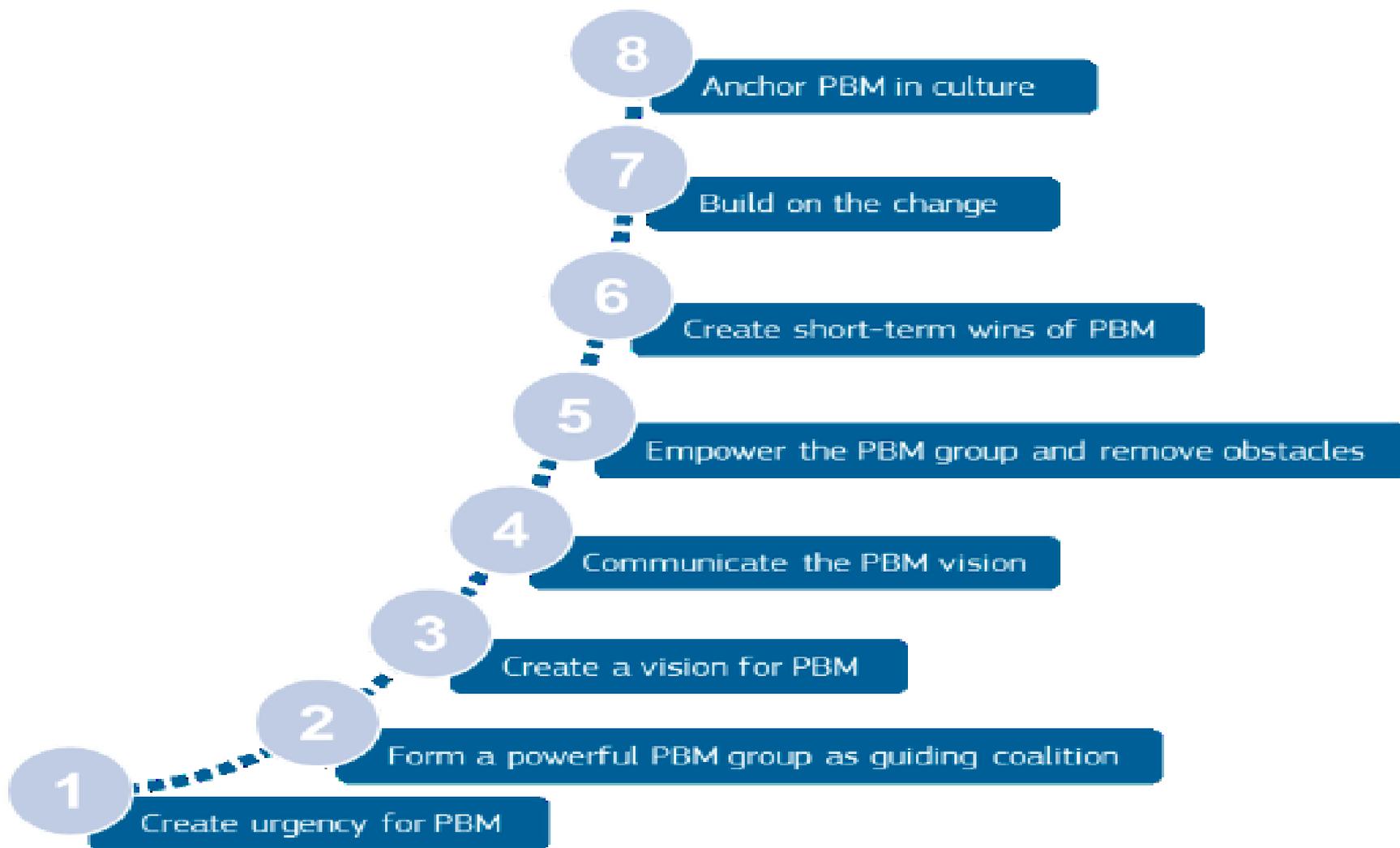
- PERCORSI TERAPEUTICI PER LA TERAPIA DI SUPPORTO (Ferrogluconato, Ferrocarbrossimaltoso, eritropoietina)



- MONITORAGGIO NON INVASIVO MULTIPARAMETRICO (fluidoterapia, parametri ossiforetici)

- Clinicians
- Clinical support
- Patient advocacy
- Public health professionals
- Implementation experts
- Hospital administration





MODELLO A 8 STEP DI KOTTER



# Supporting Patient Blood Management (PBM) in the EU

## A Practical Implementation Guide for Hospitals

Published online

August 2016



Division 10.1  
Software for  
Medical Applications



# Building national programmes of Patient Blood Management (PBM) in the EU

## A Guide for Health Authorities

Published online

August 2016

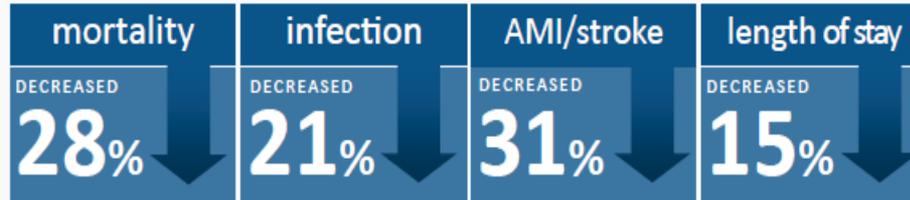


Division 10.1  
Software for  
Medical Applications

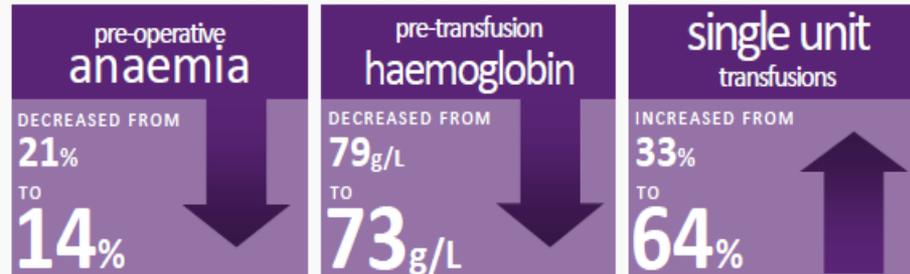
# WESTERN AUSTRALIA PATIENT BLOOD MANAGEMENT PROGRAM

The Western Australian Patient Blood Management Program recently published the world's largest study on patient blood management outcomes. The study included over 600,000 patients admitted to Western Australia's four major adult hospitals between July 2008 and June 2014. Over the six-year study period, the program was associated with:

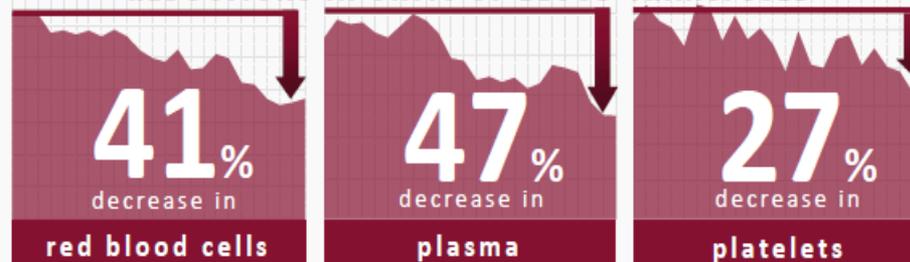
## IMPROVED PATIENT OUTCOMES



## IMPROVED KEY PROGRAM INDICATORS



## REDUCTIONS IN UNITS OF BLOOD TRANSFUSED



## PRODUCT COST SAVINGS

Over the six-year study period blood product cost savings were:

**\$18.5M**

## ACTIVITY BASED COST SAVINGS

...however with the hospital costs of administering a transfusion added, the gross savings are estimated to be between:

**\$80M – \$100M**

# *PBM GOVERNANCE*

