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Patient Blood Management Up To Date

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Perioperative Patient Blood Management Up To Date

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Conflicts of Interest

No conflict of interest for this presentation….

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Conflicts of Interest

…..unless I am an anaesthesiologist.

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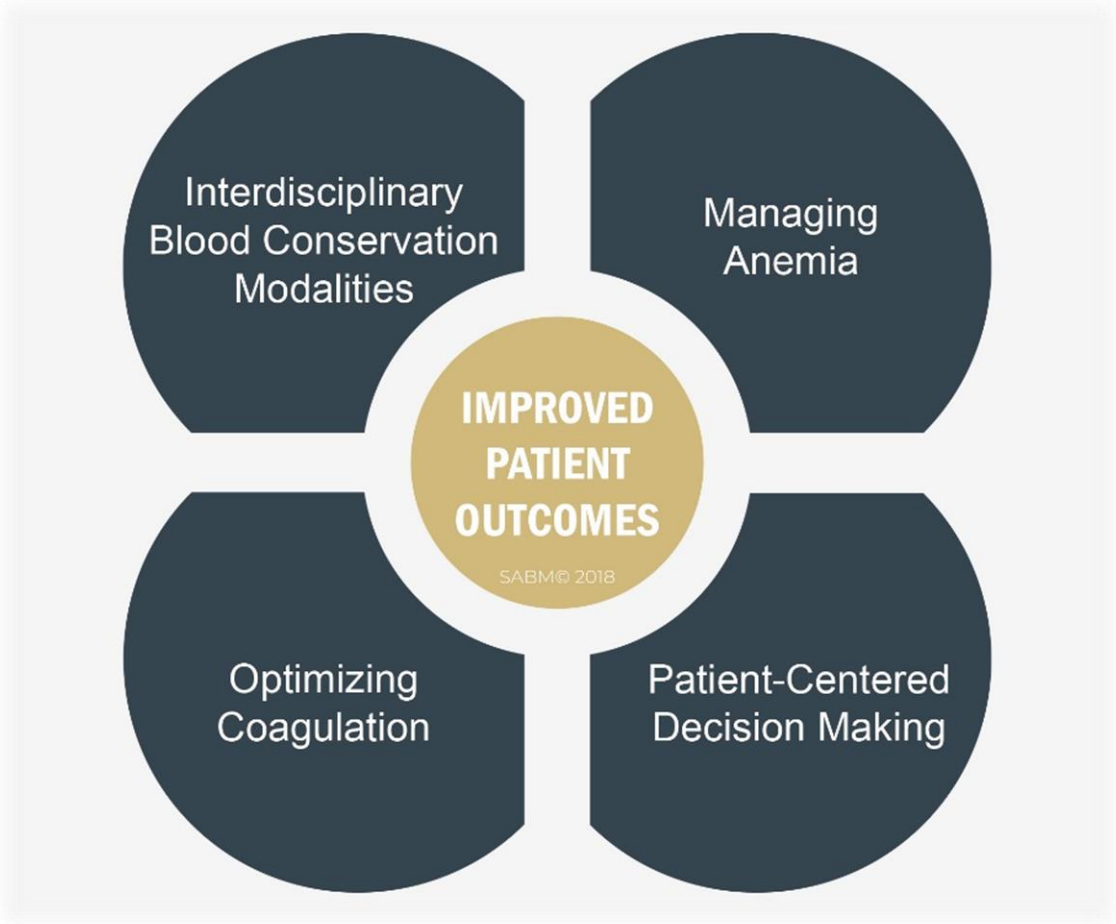
General Concepts



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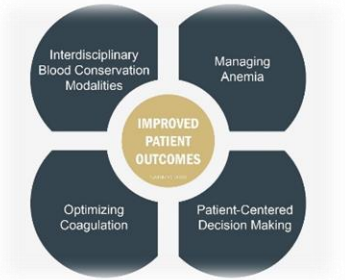
SABM Definition



Patient Blood Management is the ***timely application*** *of evidence based medical and surgical concepts designed to* ***manage anaemia, optimize haemostasis, and minimize blood loss*** *in order to* ***improve patient outcomes.***

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Multidisciplinarity

Perioperative

Preoperative Optimization

Minimal Intraoperative Blood Loss

Conservation of Postoperative Blood Volume

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Multidisciplinarity

Perioperative

GP Internist Surgeon Anesthesiologist	Anesthesiologist Surgeon OR technician Blood Service	Intensivist Surgeon Nurses GP

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Multidisciplinarity

Perioperative

GP Internist Surgeon Anesthesiologist	Anesthesiologist Surgeon OR technician **Blood Service**	Intensivist Surgeon Nurses GP

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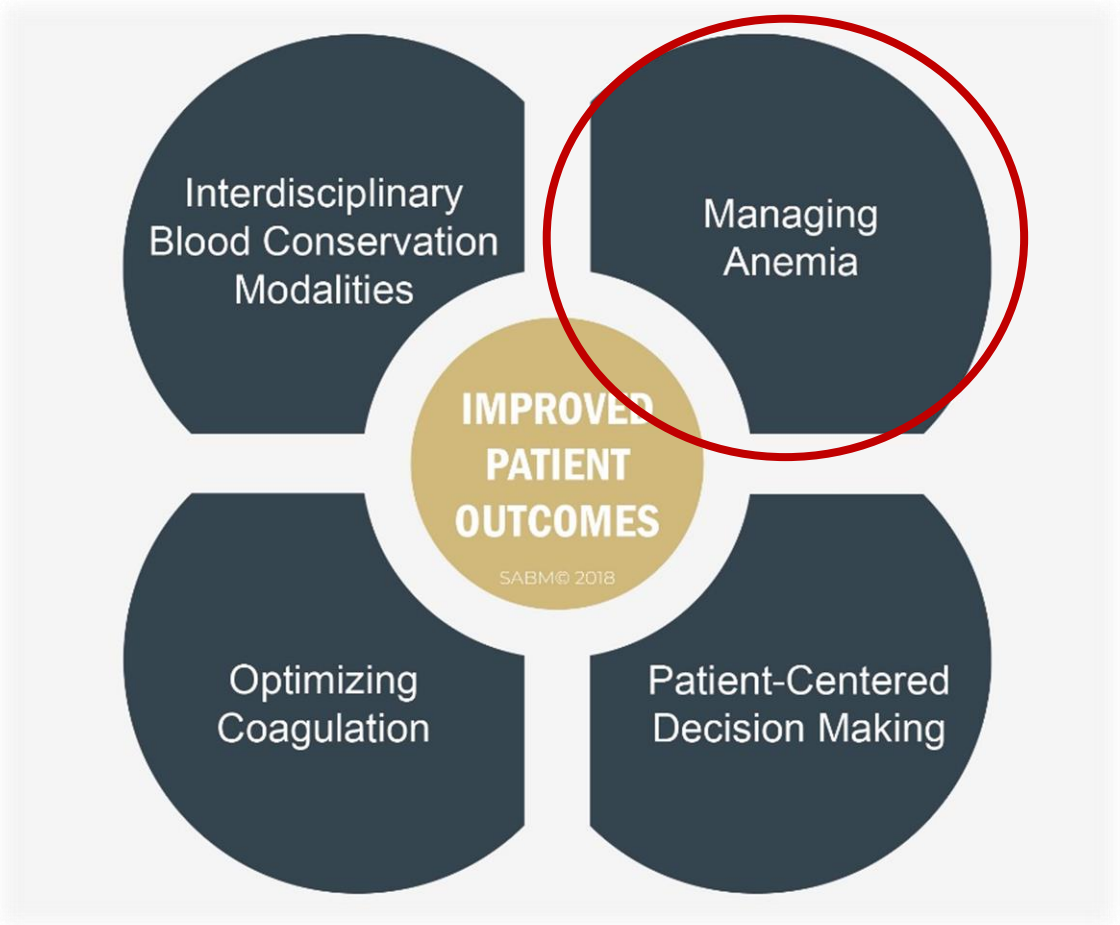
General Principles



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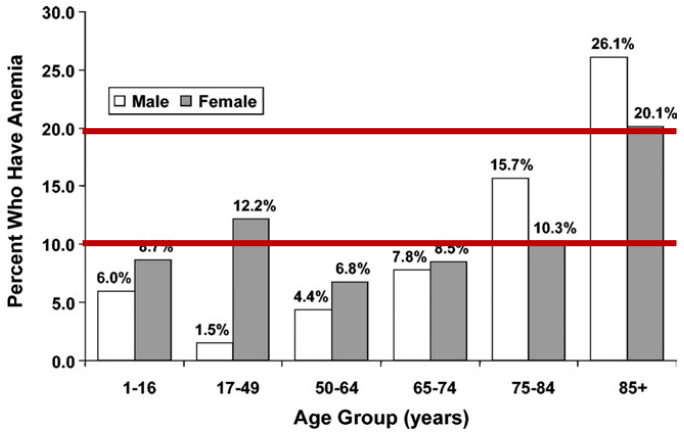
Managing Anaemia

- Anaemia is frequent.



- Anaemia is not normal and should not be accepted as a matter of fact.
- Anaemia is associated with risk of RBC transfusion and worse patient outcome.

Nhanes III study, Blood 2004

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Preoperative Anaemia

Hb <130 g/l (Men) und <120 g/l (Women)	Men	Women	Total
Elective Hip and Knee Prosthesis Surgery	13% (15/120)	30% (30/102)	20% (45/222)
Elective Major Spinal Surgery	13% (18/140)	16% (20/129)	14% (38/269)

own data, UHBS 2015

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Transfusion with RBC	Anaemic Men	Non-anaemic Men	Anaemic Women	Non-anaemic Women
Elective Hip and Knee Prosthesis Surgery	43%	10%	53%	14%
Elective Major Spinal Surgery	45%	0%	28%	7%

own data, UHBS 2015

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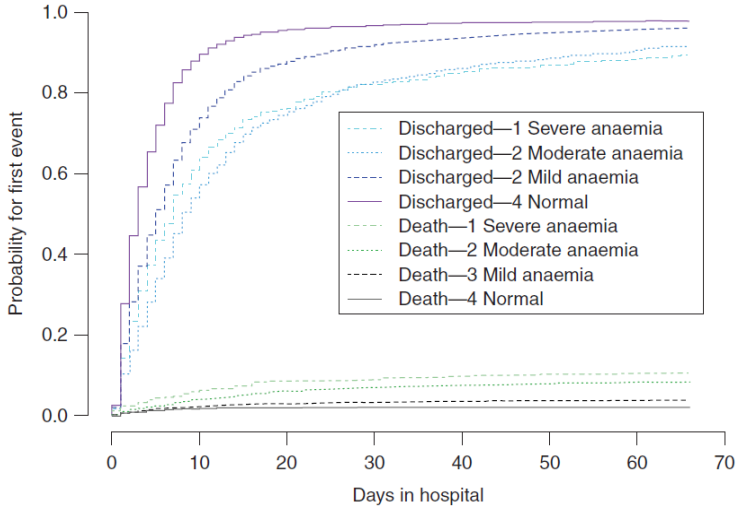
about 4x more common!!!!

own data, UHBS 2015

Anaemia and Outcome



Preoperative anaemia, even mild, is associated with:

- Higher postoperative mortality
- Higher postoperative morbidity (infections, thromboembolim, renal failure, myocardial infarction, stroke, etc.)
- Longer ICU/hospital stay
- Higher costs

Baron et al. BJA 2014, Musallam et al. Lancet 2011

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Anaemia and Outcome

Is it the cause or an association?

- Limited oxygen delivery to end organs and lower ischaemia tolerance during haemorrhage
- More blood transfusion might impair outcome
- Anaemia is a marker of severity of patient's comorbidities

Baron et al. BJA 2014, Musallam et al. Lancet 2011

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Anaemia and Outcome

Anaemia seems to be a modifiable risk factor before surgery

→ Treatment strategies:

- Stopp occult bleeding (GI)
- Iron supplementation
- Erythropoiesis-stimulating agents (ESA)
- Combination therapy

Baron et al. BJA 2014, Musallam et al. Lancet 2011

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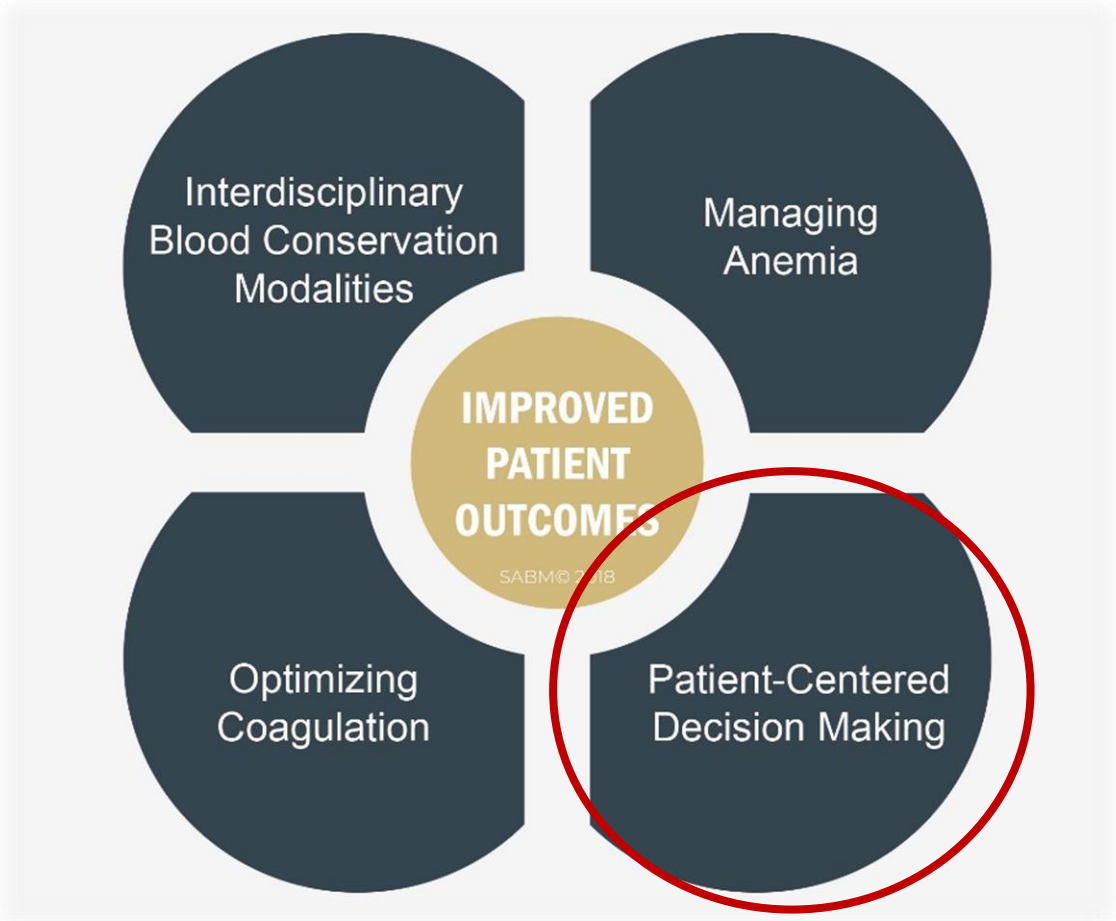
Personalized Medicine



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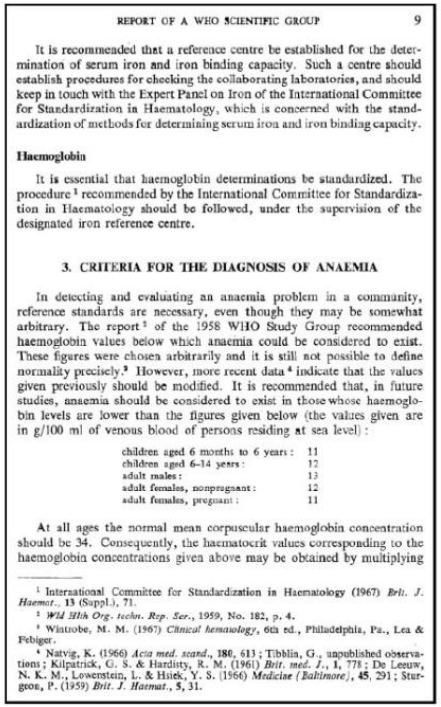
Personalized Anaemia Therapy

1. Surgical vs. non-surgical situations
   - Chronic vs. acute
   - How much time for treatment?
2. Correct Diagnosis/Differential Diagnosis
   - To specifically treat your anaemic patient
3. Social Aspect
   - Anaemia in young and healthy womens?
   - Testing in very elderly patients
4. Economy
   - Time is money
   - What is necessary/what is too much?
   - Cost-efficacy?

WHO definitions of anemia



REPORT OF A WHO SCIENTIFIC GROUP 9

It is recommended that a reference centre be established for the determination of serum iron and iron binding capacity. Such a centre should establish procedures for checking the collaborating laboratories, and should keep in touch with the Expert Panel on Iron of the International Committee for Standardization in Haematology, which is concerned with the standardization of methods for determining serum iron and iron binding capacity.

Haemoglobin

It is essential that haemoglobin determinations be standardized. The procedure [1] recommended by the International Committee for Standardization in Haematology should be followed, under the supervision of the designated iron reference centre.

3. CRITERIA FOR THE DIAGNOSIS OF ANAEMIA

In detecting and evaluating an anaemia problem in a community, reference standards are necessary, even though they may be somewhat arbitrary. The report [2] of the 1958 WHO Study Group recommended haemoglobin values below which anaemia could be considered to exist. These figures were chosen arbitrarily and it is still not possible to define normality precisely.[3] However, more recent data [4] indicate that the values given previously should be modified. It is recommended that, in future studies, anaemia should be considered to exist in those whose haemoglobin levels are lower than the figures given below (the values given are in g/100 ml of venous blood of persons residing at sea level):

children aged 6 months to 6 years:	11
children aged 6–14 years:	12
adult males:	13
adult females, nonpregnant:	12
adult females, pregnant:	11

At all ages the normal mean corpuscular haemoglobin concentration should be 34. Consequently, the haematocrit values corresponding to the haemoglobin concentrations given above may be obtained by multiplying

[1] International Committee for Standardization in Haematology (1967) *Brit. J. Haemat.*, **13** (Suppl.), 71.

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1959, No. 182, p. 4.

[3] Wintrobe, M. M. (1967) *Clinical hematology*, 6th ed., Philadelphia, Pa., Lea & Febiger.

[4] Natvig, K. (1966) *Acta med. scand.*, **180**, 613; Tibblin, G., unpublished observations; Kilpatrick, G. S. & Hardisty, R. M. (1961) *Brit. med. J.*, **1**, 778; De Leeuw, N. K. M., Lowenstein, L. & Hsieh, Y. S. (1966) *Medicine (Baltimore)*, **45**, 291; Sturgeon, P. (1959) *Brit. J. Haemat.*, **5**, 31.

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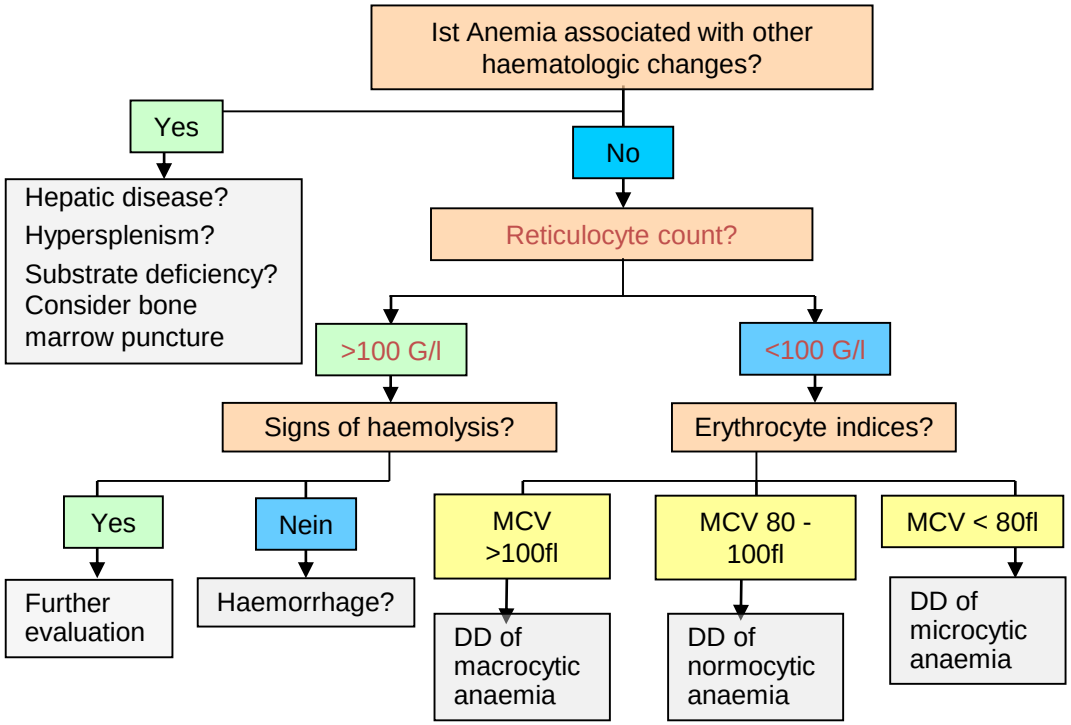
Anaemia Diagnostics

Correct Diagnosis/Differential Diagnosis

- To specifically treat your anaemic patient



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Anaemia Diagnostics

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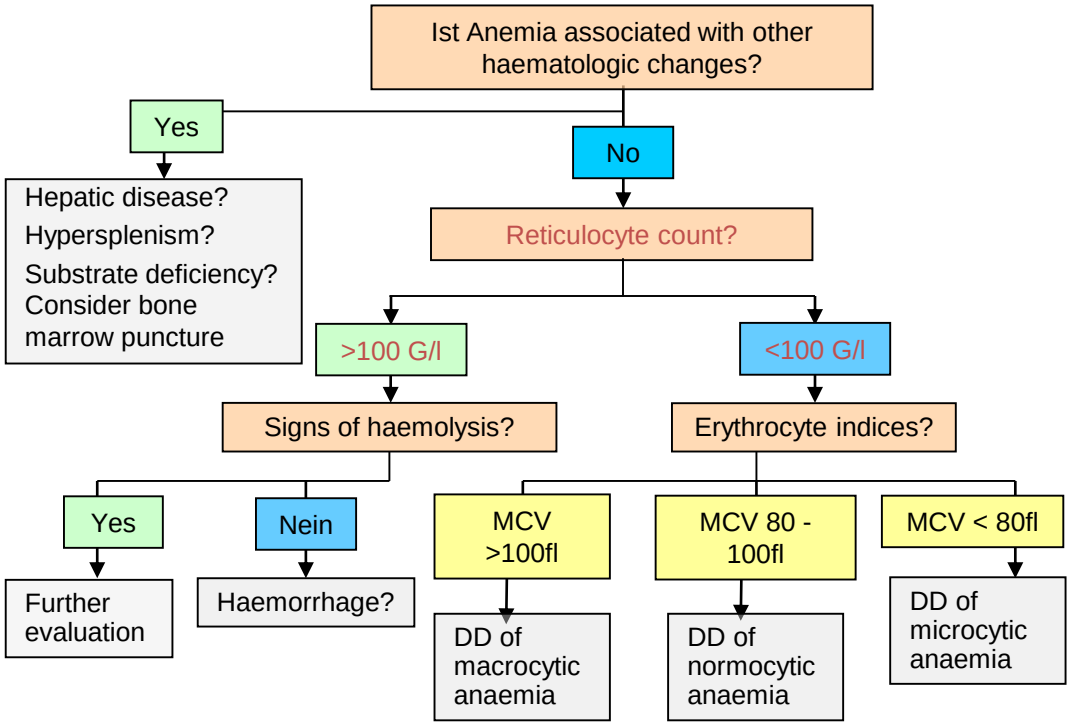

Is this feasible in your institution? Is the GP able to perform this?

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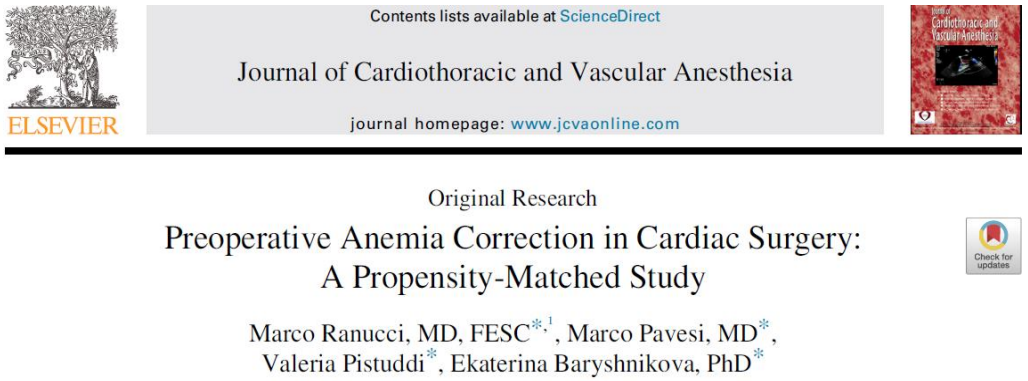
Preoperative Anaemia Clinics

Elective vs. emergent?

- Emergency?
- Time for complete anaemia testing?



Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Research

Preoperative Anemia Correction in Cardiac Surgery: A Propensity-Matched Study

Marco Ranucci, MD, FESC*,1, Marco Pavesi, MD*, Valeria Pistuddi*, Ekaterina Baryshnikova, PhD*

A recent Italian study in patients scheduled for cardiac surgery showed that only about 20% of anemic patients could be timely and correctly identified.

Ranucci et al. J Cardiothorac Vasc Anesth 2021

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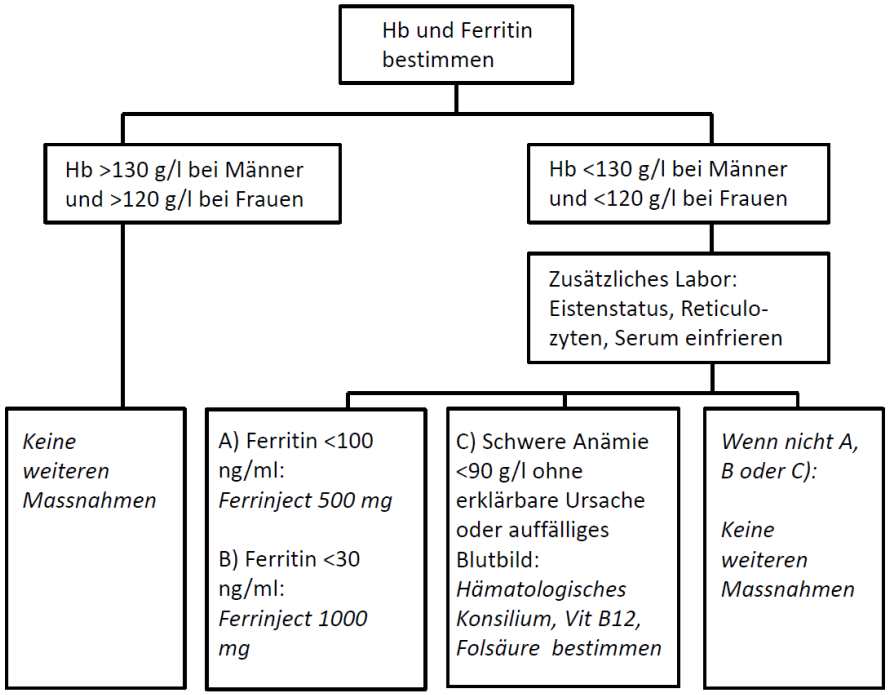
Example From Our Institution

- PBM program for major surgery
- WHO anaemia criteria
- Simplified treatment algorithm



Klöser et al. J Cardiothorac Vasc Anesth 2022 *in review*

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Example From Our Institution

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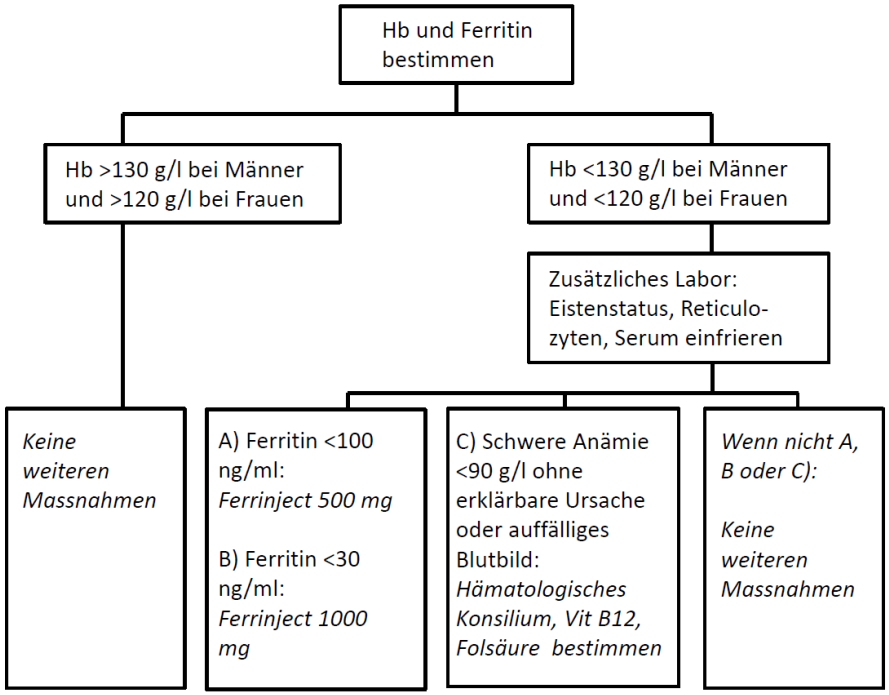
Preop Lab:

- Hb 115 g/l
- Transferrin saturation 21%, ferritin 53 microg/l, transferrin 2.23 g/l, Iron 11.7 micromol/l
- GFR 63 ml/min/1.7
- CRP 8 mg/l



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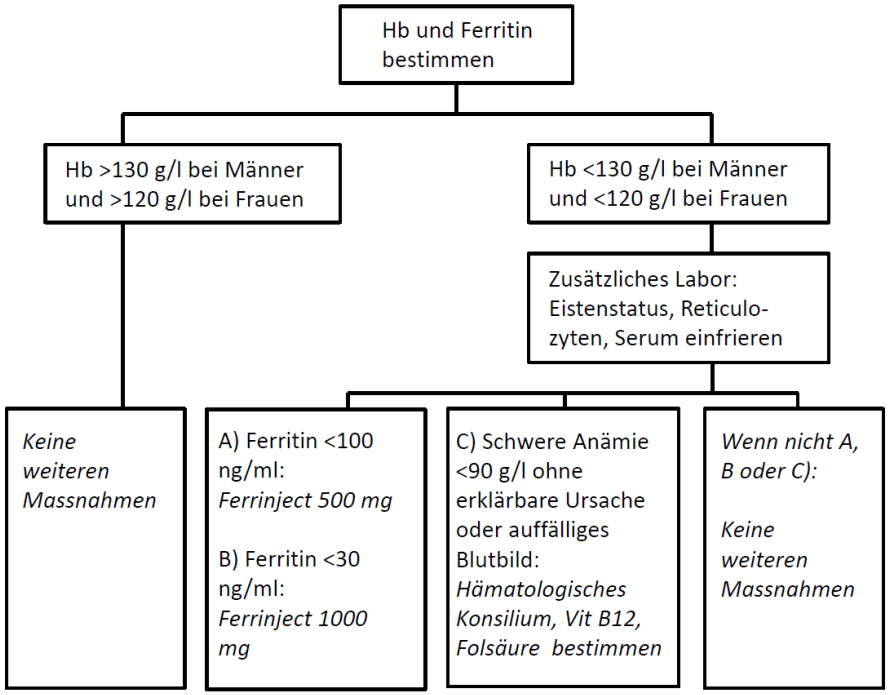

- **Highly suspicious for iron deficiency anaemia**

Klöser et al. J Cardiothorac Vasc Anesth 2022 *in review*

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PREVENTT Trial

Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, double-blind, controlled trial

Participants: 487 patients from 46 UK hospitals with preop anaemia (M <130 g/l, F <120 g/l), scheduled for major open abdominal surgery

Intervention: 1 g Fe-Carboxymaltose (Ferinject) or Placebo, 1:1-randomization, double-blinded; 10-42 days before surgery

Primary Endpoints: Death or blood transfusion within 30 days; blood transfusion within 30 days after surgery; number of transfused blood products

Results: 29% vs. 28% (RR 1.03; 95% CI 0.78-1.37); 105 vs. 111 transfusions (RR 0.98; 95% CI 0.68-1.43)

Conclusions: Preoperative administration of iron before major abdominal surgery does not reduce the transfusion of blood products

Richards et al. Lancet 2020

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Criticism to PREVENTT

- «Pragmatic Trial»
- No diagnostics on iron deficiency anaemia before inclusion
- 70% of patients had no simple iron deficiency anaemia
- Median treatment was 15 days before surgery, ideally 25-50 days
- «Transfusion of blood products» include RBC, FFP, platelets
- Not transfusion algorithm, no haemostasis algorithm
- Many hospitals, low number of patients per institution
- «Long term effect» such as re-hospitalizationen and higher haemoglobin after 8 weeks and 6 months evident but hardly discussed

Hardy et al. Anesth Analg 2021

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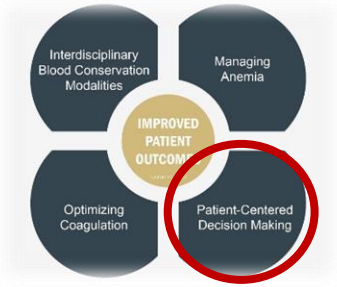
Anaemia of Chronic Disease



- Infections, acute or chronic
- Autoimmun diseases
- Malignancies
- «Critically ill» patients
- Heart failure
- Chronic renal insufficiency
- Adipositas, metabolic syndrome
- Age (Anaemia of the elderly)

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Therapeutic Options in Multifactorial Anaemia

1. Therapy/Control of infection or inflammatory disease

- In up to 30% of cases, there is evidence for an inflammatory etiology

2. Iron substitution

- Parenteral
- Potentially repeated small doses more effective than one conventional dose, for exmaple
  - Venofer® 200 mg 1-2/Woche for 3-4 weeks
  - Ferinject® 100-500 mg 1x/Woche for 3-4 weeks

3. Stimulation of erythropoiesis

- Epoetin® 10’000E 1x/week or 20’000E 1x/2 weeks
- Darbepoetin® 6.75 µg/kg, 1x/3 weeks

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«Ultra-Short-Treatment» Study

Effect of ultra-short-term treatment of patients with iron deficiency or anaemia undergoing cardiac surgery: a prospective randomised trial

Donat R Spahn, Felix Schoenrath*, Gabriela H Spahn, Burkhardt Seifert, Philipp Stein, Oliver M Theusinger, Alexander Kaserer, Inga Hegemann, Axel Hofmann, Francesco Maisano, Volkmar Falk*

Participants: 505 anaemic patients (WHO criteria) or iron deficiency (Ferritin <100 µg/l); scheduled for cardiac surgery

Intervention: 20 mg/kg Fe-Carboxymaltose (Ferinject) iv + 40'000 E Erythropoeitin alpha sc + 1 mg Vit B12 sc + 5 mg folic acid po or placebo **on the day before surgery**

Primary Endpoint: Number of transfused RBCs within the first 7 days

Results: 0 [IQR 0-2] vs. 1 [IQR 0-3] (p=0.038), less transfusion up to 90 days after surgery

Conclusions: A «ultra-short» combination therapy on the day before surgery reduces blood transfusion in cardiac surgery patients

Spahn et al. Lancet 2019

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Strengths and Weaknesses

- «pragmatic trial»
- Feasible for most institutions
- Positive findings (less RBC transfusion)

aber:

- Cumbersome (several stiches and infusions)
- Very expensive, not paid by insurancies in Switzerland
- Cost efficacy must be re-evaluated

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Can We Improve Outcome?

Patient blood management interventions do not lead to important clinical benefits or cost-effectiveness for major surgery: a network meta-analysis

Marius A. Roman[1,*], Riccardo G. Abbasciano[1], Suraj Pathak[1], Shwe Oo[2], Syabira Yusoff[1,*,7], Marcin Wozniak[1], Saqib Qureshi[3], Florence Y. Lai[1], Tracy Kumar[1], Toby Richards[4], Guiqing Yao[5], Lise Estcourt[6] and Gavin J. Murphy[1]

Methods: Systematic review and update for five former systematic reviews and a NICE health economic reviews of common PBM interventions; network meta-analysis

Results: 393 eligible RCTs enrolling 54 917 participants. PBM interventions resulted in reduced exposure to RBC transfusion (RR 0.60; 95% CI 0.57-0.63) and slightly shorter ICU/hospital length of stay; no effect on mortality (RR=0.93; 95% CI 0.81-1.07), AKI, infection/sepsis, low cardiac output, myocardial infaction, and acute brain injury.

Conclusions: In RCTs, PBM interventions had no important clinical benefits beyond reducing bleeding and transfusion in major surgery

Roman et al. BJA 2021

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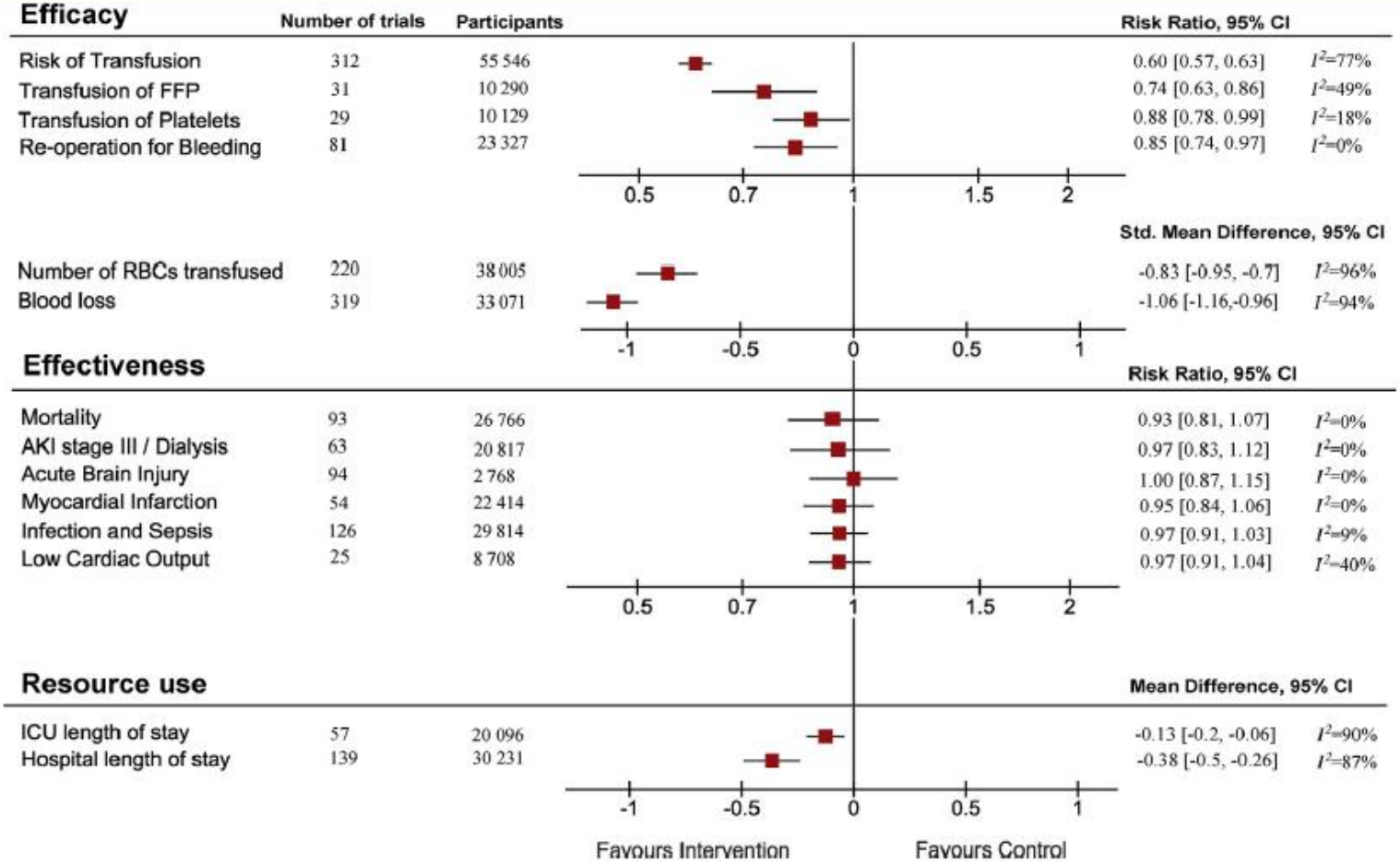
Can We Improve Outcome?



Roman et al. BJA 2021

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Cost Efficacy of PBM

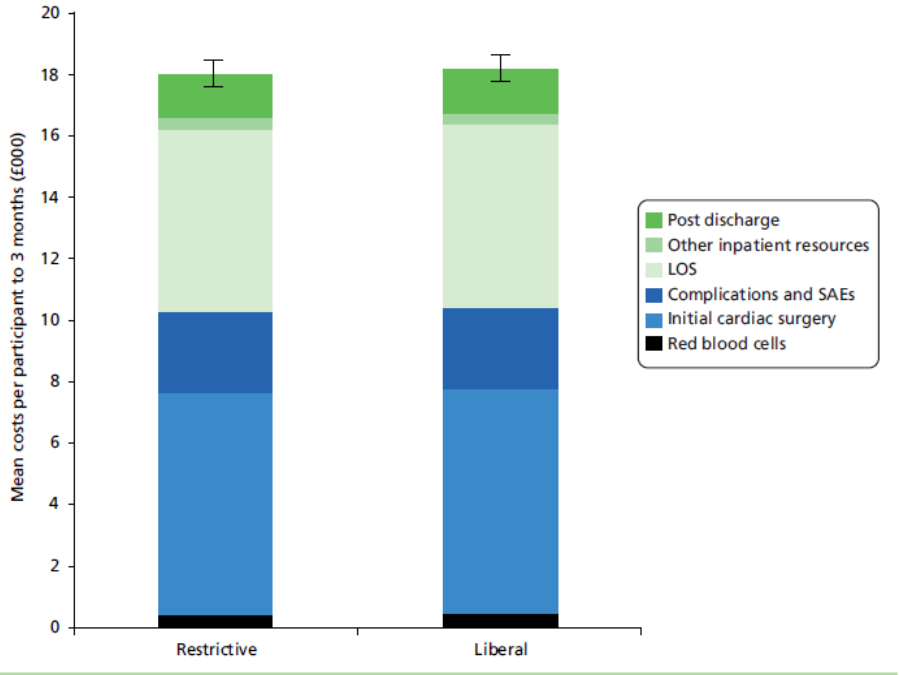

FIGURE 17 Breakdown of total costs for each treatment group. Error bars show SEs around total costs.

2007 patients undergoing cardiac surgery in the UK, randomized to restrictive or liberal RBC transfusion after CPB

3-month costs:
17'945 £ vs. 18'127 £

Questionable cost effectiveness but blood is a valuable and precious ressource.

Reeves et al. Health Techn Assessment 2016

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Take Home Message

- Preoperative anaemia is common and has relevant impact on patient outcome
- PBM is an important concept aiming to improve patient outcome
- PBM interventions reduces exposure to blood products (mainly RBC) but evidence for further positive effects on patient morbidity and mortality is scarce at the moment
- Cost-effectiveness is questionable but blood products remain a precious and limited ressource

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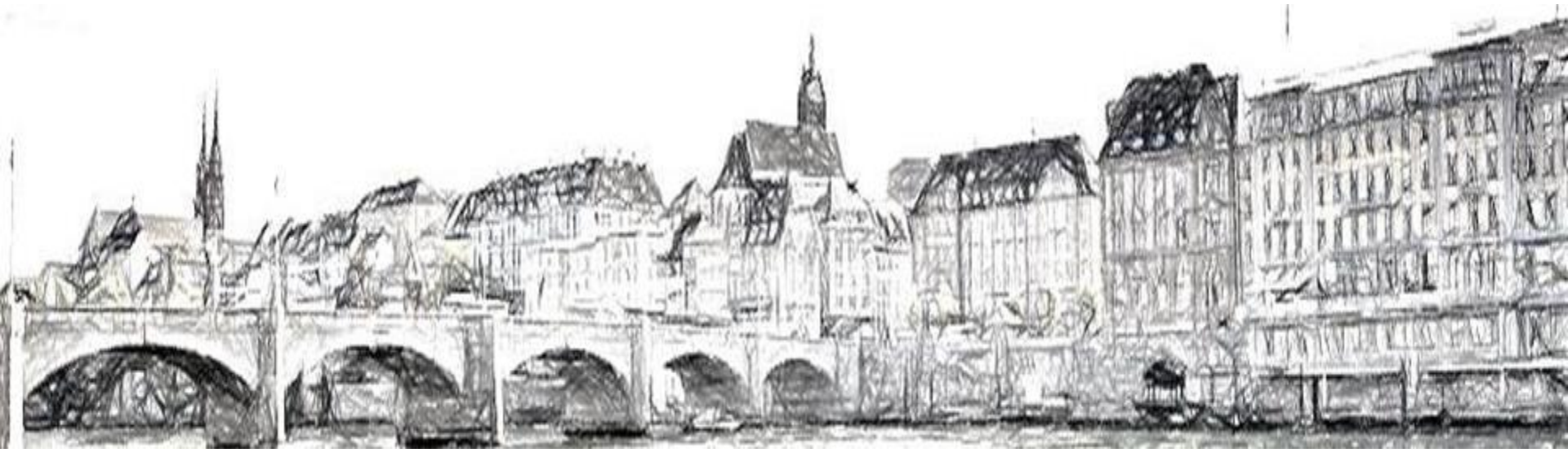
Thank You For Your Attention