

BHS training course and seminars



BHS

Belgian Hematology Society

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**seminar n°5: transfusion
and cell therapy**

**2th MARCH
2024**

Transfusion indications

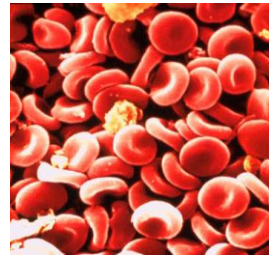
(RBC, platelets, plasma)

AND

Patient Blood Management

Timothy Devos (UZ Leuven)

Indications for erythrocyte transfusions (ECL)



General rules transfusion



- **only transfuse if the risk of not-transfusing > risk of the transfusion (risk-benefit)**
- **carrying out a transfusion is NOT only decided by a lab value, always evaluate the clinical condition of the patient**
- **there is no magic ‘transfusion threshold’**

Trigger Hb concentration



- **Hb \geq 9 g/dl** → rarely a transfusion is needed
- **Hb 7-9 g/dl** → low risk of hypoxic organ damage in most of the patients: « **Why transfuse ?** ». Decision determined by clinical condition.
- **Hb $<$ 7 g/dl** → substantial risk of hypoxic organ damage: « **Why not transfuse ?** »
- **Hb $<$ 4.5 g/dl** → life of the patient is in immediate danger.

Other factors

- **duration of anemia (acute versus chronic)**
- **clinical evaluation: cardiovascular, pulmonary, cerebral status** → risk of volume overload ?
- **possibility of acute bleeding ?**





Going towards more restrictive transfusion thresholds



TRICC-trial: transfusion requirement in critical care

TABLE 3. COMPLICATIONS THAT OCCURRED DURING THE PATIENTS' STAYS IN THE INTENSIVE CARE UNIT.

COMPLICATION*	RESTRICTIVE-TRANSFUSION STRATEGY (N=418)	LIBERAL-TRANSFUSION STRATEGY (N=420)	ABSOLUTE DIFFERENCE BETWEEN GROUPS	95% CONFIDENCE INTERVAL†	P VALUE
	no. (%)	no. (%)	percent	percent	
Cardiac	55 (13.2)	88 (21.0)	7.8	2.7 to 12.9	<0.01
Myocardial infarction	3 (0.7)	12 (2.9)	2.1	—	0.02
Pulmonary edema	22 (5.3)	45 (10.7)	5.5	1.8 to 9.1	<0.01
Angina	5 (1.2)	9 (2.1)	0.9	—	0.28
Cardiac arrest	29 (6.9)	33 (7.9)	0.9	-2.6 to 4.5	0.60
Pulmonary	106 (25.4)	122 (29.0)	3.7	-2.3 to 9.7	0.22
ARDS	32 (7.7)	48 (11.4)	3.8	-0.2 to 7.8	0.06
Pneumonia	87 (20.8)	86 (20.5)	-0.3	-5.8 to 5.1	0.92
Infectious	42 (10.0)	50 (11.9)	1.9	-2.4 to 6.1	0.38
Bacteremia	30 (7.2)	40 (9.5)	2.3	-1.4 to 6.1	0.22
Catheter-related sepsis	21 (5.0)	17 (4.0)	-1.0	-3.8 to 1.8	0.50
Septic shock	41 (9.8)	29 (6.9)	-2.9	-6.7 to 0.8	0.13
Hematologic‡	10 (2.4)	10 (2.4)	0	-2.1 to 2.1	1.00
Gastrointestinal§	13 (3.1)	19 (4.5)	1.4	-1.2 to 4.0	0.28
Neurologic¶	25 (6.0)	33 (7.9)	1.9	-1.6 to 5.3	0.28
Shock	67 (16.0)	55 (13.1)	-2.9	-7.7 to 1.8	0.23
Any complication	205 (49.0)	228 (54.3)	5.2	-1.5 to 12.0	0.12

n = 838

inclusion:

Hb < 9g/dl during first 72h of admission

duration of study 30 days:

- restrictive group:
2.6 ECL per patient

- liberal group:
5.6 ECL per patient

reduction of 56 %

primary endpoint:

30 days mortality (all causes)

- 'restrictive' group: ECL if Hb < 7 g/dl, target Hb 7-9 g/dl
- 'liberal' group: target Hb 10-12 g/dl

RESULTS TRICC TRIAL

- significantly more pulmonary edema and AMI in the 'liberal group' (cfr table 3)
- mortality D30: restrictive group 18.7% - liberal group 23.3 % (p = 0.11)
- survival significantly better in 2 subgroups of the restrictive group:
 - APACHE II score ≤ 20
 - age < 55 yr

CONCLUSION:

TRICC trial: euvolemic intensive care adult patients benefit from a restrictive transfusion approach

→ aim: Hb concentrations between 7.0 and 9.0 g/dl

FOCUS trial: hip surgery and ECL transfusion

- aim: study safety of restrictive transfusion strategy in older (hip-) surgery patients with history of or risk factors for cardiovascular disease.
- n = 2016; ≥ 50 yr; Hb < 10 g/dl post-surgery
- **restrictive (Hb: 8 g/dl)** vs. liberal (Hb: 10 g/dl)
- **restrictive groep: 3 x less ECL**
- **no outcome difference** (primary outcome) = mortality or inability to walk around a room without human assistance on D60.
- **number of complications equal in both groups**



NEJM 2011; 365: 2453-62

Patient Blood Management
Recommendations From the
2018 Frankfurt Consensus Conference

Red Blood Cell Transfusion
2023 AABB International Guidelines

RBC transfusion (ECL) **threshold Hb < 7.0 g/dL** for:

- critically ill and clinically stable patients (Hb < 7.0 g/dL) **(also hospitalized, stable adult patients with hematologic and oncologic disorders)**
- hemodynamically stable patients with acute gastrointestinal bleeding (Hb 7.0 g/dL)

RBC transfusion (ECL) **threshold Hb < 7.5 g/dL**:

- “in accordance with the restrictive strategy threshold used in most trials, clinicians may choose a threshold of 7.5 g/dL for patients undergoing cardiac surgery.”

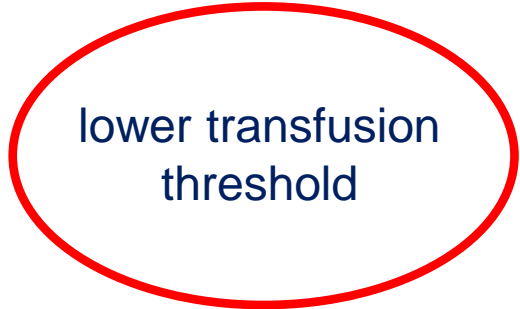
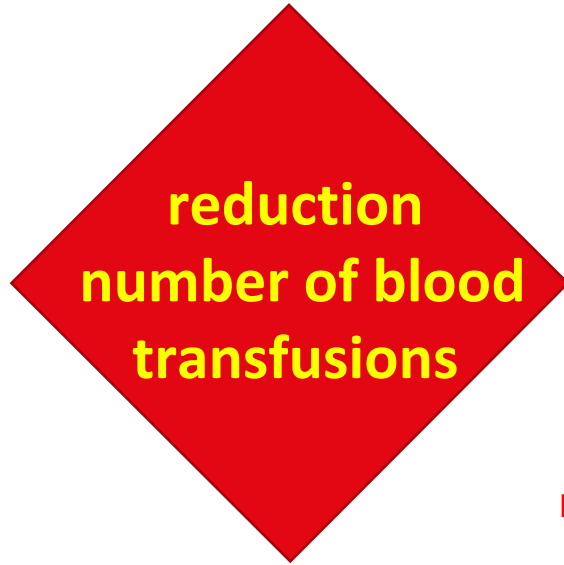
RBC (ECL) transfusion **threshold Hb < 8.0 g/dl**

- for those undergoing orthopedic surgery or those with preexisting cardiovascular disease.
- chronic CV disease or ongoing acute coronary syndrome (ACS)

erythropoietin stimulating agent (ESA)



bloodsaving surgical techniques, cell savers, ...



restrictive transfusion strategy

lower volume per transfusion
= single unit policy

Special requirements for ECL

- 1) irradiated ECL
- 2) CMV-negative blood components (ECL)
- 3) washed erythrocytes (ECL)

Indications for platelet transfusions



General rules

- **platelet transfusions improve haemostasis in thrombocytopenic patients**
- **70 % of the platelet transfusions: prophylactic**
- **if chronic BP transfusions: monitor efficacy !**
- **pooled random donor BP or single donor BP: therapeutically equivalent**

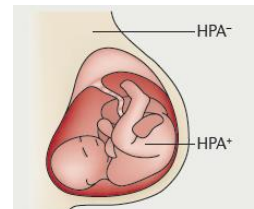
Indications platelet transfusions

- **before surgery or invasive procedures in thrombocytopenic patients** (transfusion threshold discussed later)
- **stable chronic thrombocytopenia (MDS, AA, other): but → keep a low transfusion threshold to avoid HLA-immunisation.**
- **massive transfusion: general agreement that the BP should not drop below 50.000/ μ l.**

Indications platelet transfusions (2)



- **ITP (immune mediated thrombocytopenia):** only if life threatening bleeding. BP transfusions will then be combined with Ivlg and steroids.
- **DIC:** in case of active bleeding or at high risk of bleeding: maintain BP > 50.000/ μ l
- **neonatal immune thrombocytopenia:** in addition to high dose Ivlg, HPA-compatible platelets may be required
(maintain BP count > 30.000/ μ l)



Development of HPA-specific alloantibodies and subsequent fetal and neonatal thrombocytopenia

NOT an indication

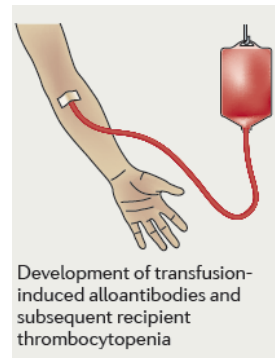


Make a NOTE of This!

EXCEPTIONS!!

➤ **ITP if no life threatening bleeding**

➤ **post transfusion purpura (PTP):
high dose Ivlg = treatment of choice**



➤ **heparin-induced thrombocytopenia (HIT): contra-indication (risk of inducing arterial or venous thrombosis)**

NOT an indication (2)



- **thrombotic thrombocytopenic purpura (TTP): contra-indication.**
 - ✓ safer not to transfuse blood platelets
 - ✓ only risk-benefit if catheterisation needed (pre-apheresis)
 - ✓ consider BP transfusion if life threatening bleeding

- **hypersplenism**

optimal prophylactic trigger for platelet TF ?

4 prospective randomised trials

3 non-randomised studies:

10,000/ μ L Platelet Transfusion Trigger					
Major Bleeding (%)	Hemorrhagic Deaths	Platelet Transfusions		Units Per Thrombocytopenic Day	Reference
		Units			
		Concentrates	Apheresis		
14	0				20
22	1				21
18	0	15.45 (0-152)	3.0± (0-16)		22
0	0				23
12	3	545 (0-647)		0.55 (0-6.94)	24
15	0			0.42	25
42	0				26

20,000/ μ L Platelet Transfusion Trigger					
Major Bleeding (%)	Hemorrhagic Deaths	Platelet Transfusions		Units Per Thrombocytopenic Day	Reference
		Units			
		Concentrates	Apheresis		
17	0				20
20	0				21
17	0	25.4 (0-180)	4.8 (0-33)		22
0	0				23
14	4	73 (3-943)		0.8 (0.03-30)	24
18	0			0.49	25
30	0				26

➤ 10.000/ μ l as safe as 20.000/ μ l

➤ less platelet transfusions given when trigger 10.000/ μ l

20. Zumber et al. *BBMT* 2002

21. Rebulla et al. *NEJM* 1997

22. Wandt et al. *Blood* 1998.

23. Heckman et al. *JCO* 1997.

24. Gil-Fernandez et al. *BMT* 1996.

25. Lawrence et al. *Leuk Lymph* 2001.

26. Navarro et al. *Haematologica* 1998.

Slichter et al. Transfus Rev Med 2004

prophylactic versus therapeutic ?

- **TOPSS** (Trial Of Prophylactic Platelets Study)

- non-inferiority study (randomized, open label)
- **non-prophylactic (therapeutic) versus prophylactic**
- hematological patients (70% autologous stem cell Tx in both study arms)

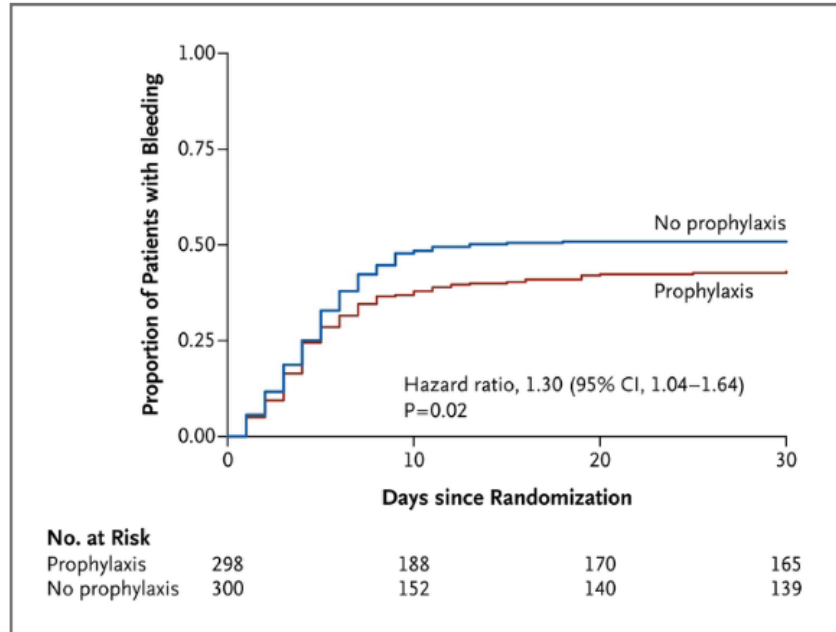
- ❖ **np-arm: 59% receiving BP-transfusions**

- ❖ **p-arm: 89% receiving BP-transfusions**

TOPSS trial

➤ results:

- time to first grade 2-4 bleeding: significantly shorter in **np-arm**
- **np-arm:** more days with grade 2-4 bleedings in comparison with p-arm (*median 1.7 d vs. 1.2 d*)



Stanworth et al. NEJM 2013

- WHO grade 2-4 bleedings: 50% in np-arm; 43 % in p-arm (*p value for non-inferiority 0.06*)
- ➔ **non-inferiority of non-prophylactic (= therapeutic) BP-transfusion strategy NOT shown !**
- (*subanalysis auto HPC Tx: 47% gr 2-4 bleedings in np-arm vs. 45% in p-arm*)

Transfusion trigger platelet transfusion

- keep **BP > 10.000/ μ l** if no risk factors for bleeding
- keep **BP > 20.000/ μ l** if risk factors for bleeding (fever, sepsis, ...)
- acute or recent important bleeding: keep **BP > 50.000/ μ l**
- therapeutic dose op LMWH: keep **BP > 50.000/ μ l**
- surgical intervention: **BP > 50.000/ μ l**
- less invasive procedures (DVC, transjugular liverbiopsy):
BP > 30.000/ μ l
- major surgical procedures (CNS): keep **BP > 100.000/ μ l**
(talk with the surgeon !)

Indications for the transfusion of plasma (FFP)



indications plasma transfusions

➤ patients with massive bleeding (life-threatening) caused by trauma or surgery:

(despite the lack of randomised controlled trials)

- plasma should be given in adequate amounts to prevent further bleeding (10-15 ml/kg). Repeat if the bleeding persists.
- at the same time: control source of bleeding, correct other factors leading to coagulopathy (acid-base disorders, hypothermia, hypocalcemia, anemia, thrombocytopenia).

➤ bleeding in patients with disturbed coagulation tests (or thrombolysis)

➤ bleeding in patients on coumarine anticoagulants:

- Prothombin complex concentrates (PCC) (PPSB or Octaplex®) are treatment of choice, together with vitamine K.
- administration of plasma can be taken into consideration when PCC not available

indications plasma transfusions (2)

- **DIC: plasma can be taken into consideration for patients with DIC who are actively bleeding. NOT in order to correct abnormal coagulation tests.**
- **severe hypofibrinogenemia: infuse several plasma units !**
- **drug induced hypofibrinogenemia (e.g. asparaginase in ALL): 4 units are given if fibrinogen < 1 g/L.**
- **TTP: supply of the missing metalloproteinase enzyme (ADAMTS-13)!**

indications plasma transfusions (3)

- **isolated factor V or XI deficiency: also prophylactic**
(cfr reimbursement criteria)
- **neonatal exchange transfusions in case of ABO incompatibility**

NOT an indication for plasma transfusions

- **prophylactic plasma transfusions to patients with normal coagulation tests, submitted to high-risk surgery or invasive diagnostic procedures.**
- **volume expansion (in spite of being a good volume expander; we have colloids and cristalloids for that !)**
- **plasma exchange: use albumin or crystalloids !**

Patient Blood Management (PBM)

PBM

Evidence-based, multidisciplinary, patient-centered, multimodal approach → to optimise care of patients who might need transfusion

= Bundle of care

⇒ Goal = to improve patient outcome

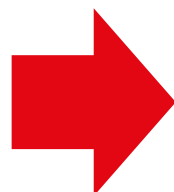
Focus shift

Blood safety

Product-centered



Hemovigilance,
Transfusion
appropriateness

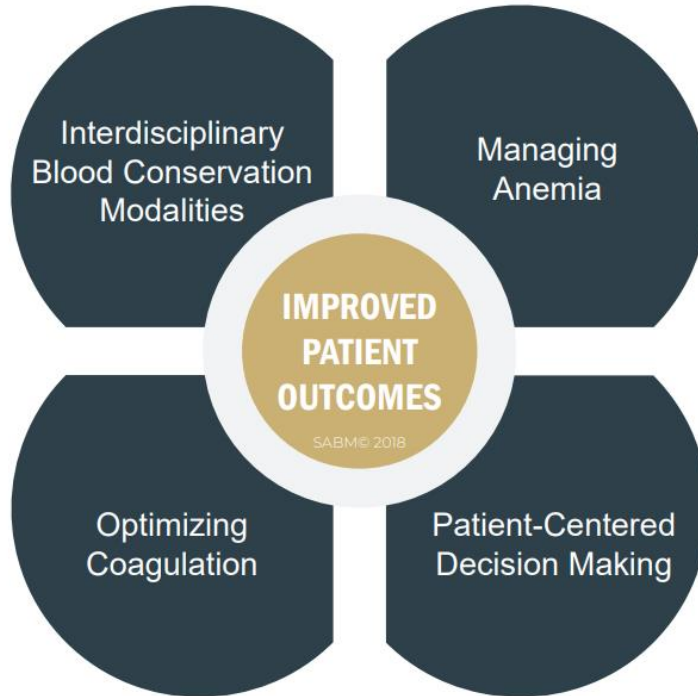


PBM

Patient-centered

PBM: proactive application of 4 leading principles

bloodsaving surgical techniques, cell savers, avoid blood overdraw, ...



optimize pre-operative anemia, ...

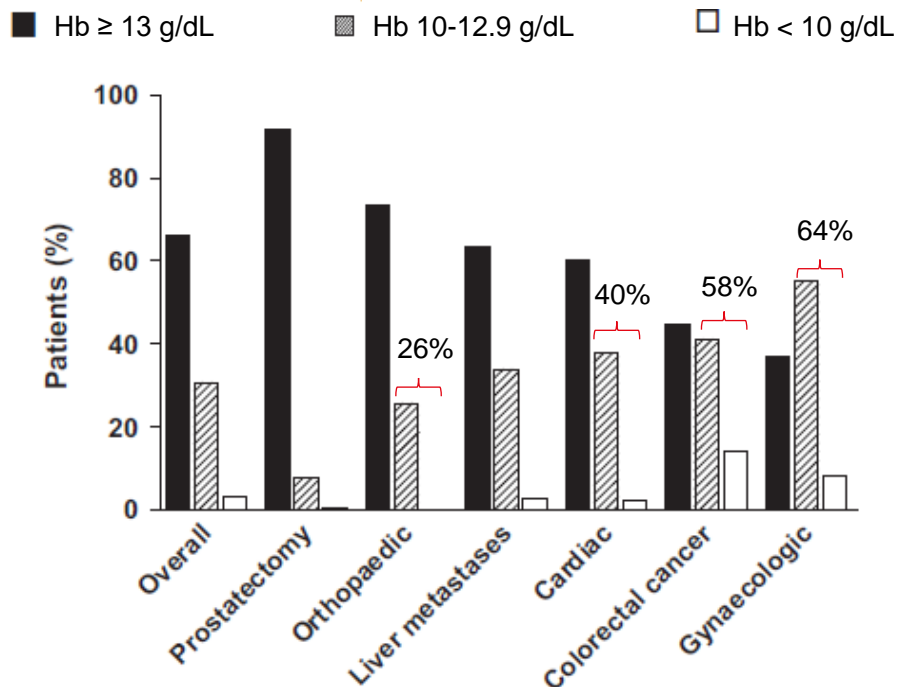
evidence based indications for TXA (tranexamic acid),

improved (or stable) clinical outcomes, expose patients to less transfusion risk, ...

Source: SABM

Prevalence of preoperative anemia

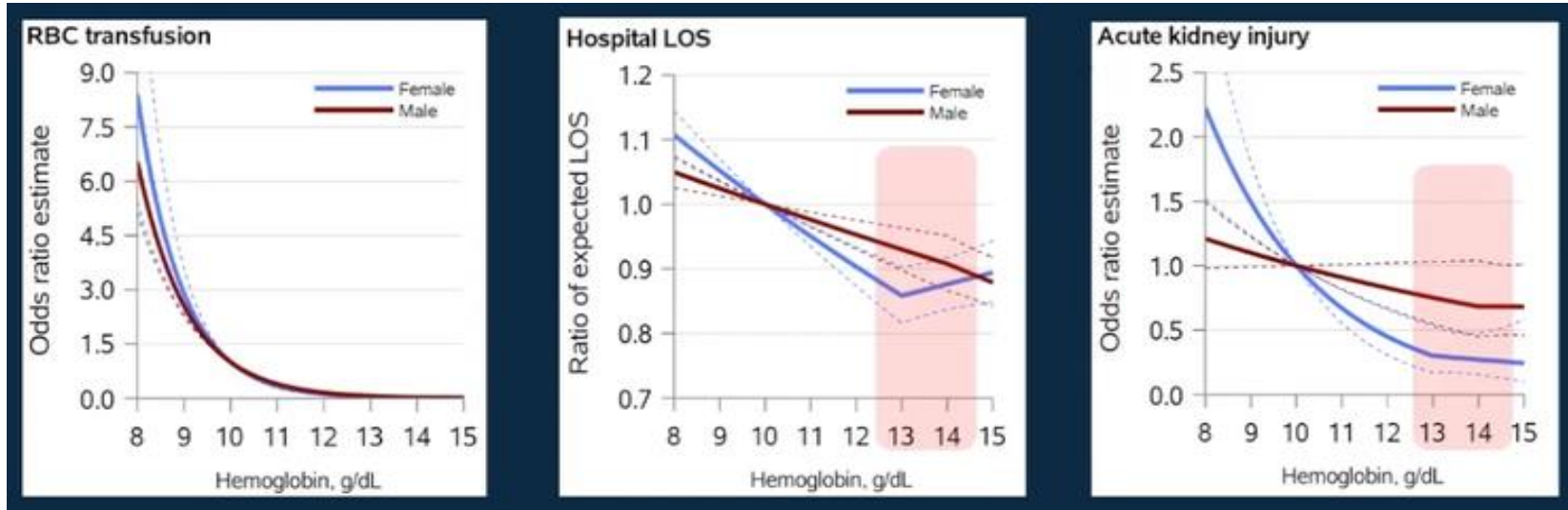
n= 3342 patients undergoing major surgery



- Overall prevalence of **anemia = 36%** ((Hb < 13 g/dL for both sexes)
- differences according to the type of surgery
- off anemic patients:
 - 62% had absolute Fe deficiency
 - 10% had Fe sequestration (chronic disease)

Impact of preoperative anemia

Preoperative anemia associated with **inferior outcome** after cardiac surgery

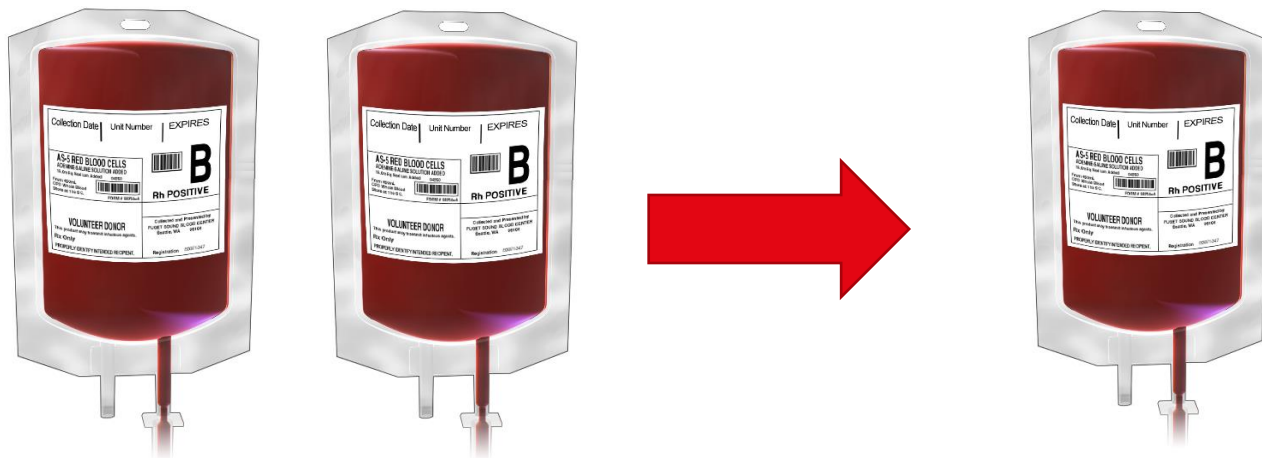


More RBC transfusion

Longer hospital stay

Higher risk of acute kidney injury

single unit policy



Single unit transfusion policy

Stable, non-bleeding, hospitalized, adult patients with symptoms of anemia

Transfuse
1



- patients with Hb concentrations close to the threshold should receive 1 RBC unit

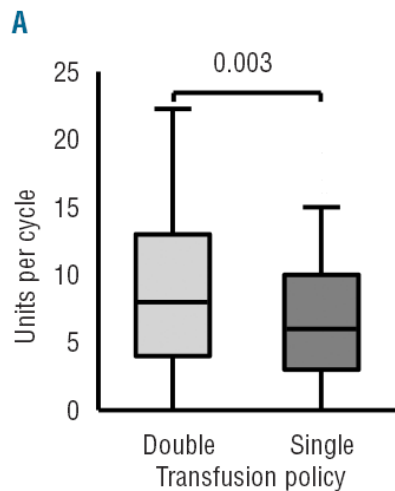
and
reassess

- then they should be reassessed **clinically** (did heart rate slow down, did blood pressure improve, etc)?
- and with a **laboratory** measurement of their **Hb** concentration following the transfusion of the first RBC unit.

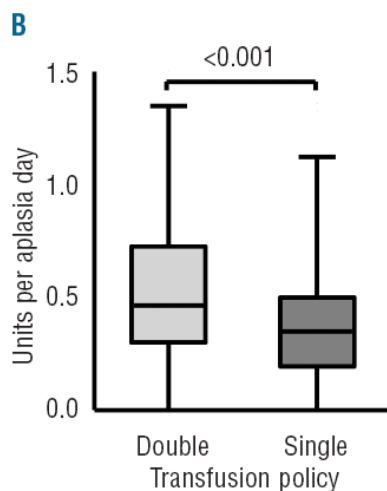


If the first unit did not lead to the desired improvement in clinical and/or in lab value, then they can have a second unit

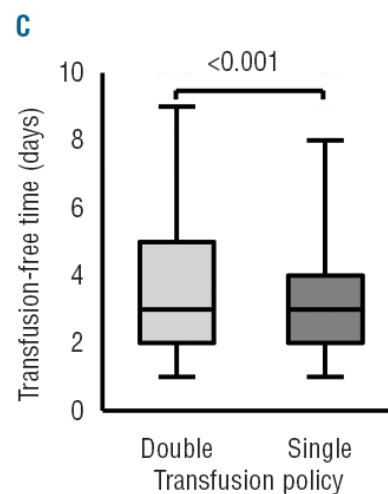
Single unit policy



25% reduction
(-2.7 unit) of RBC
transfusions per
therapy cycle




24% reduction
of RBC transfusions
per aplasia day



Median time between
transfusions **20%**
shorter

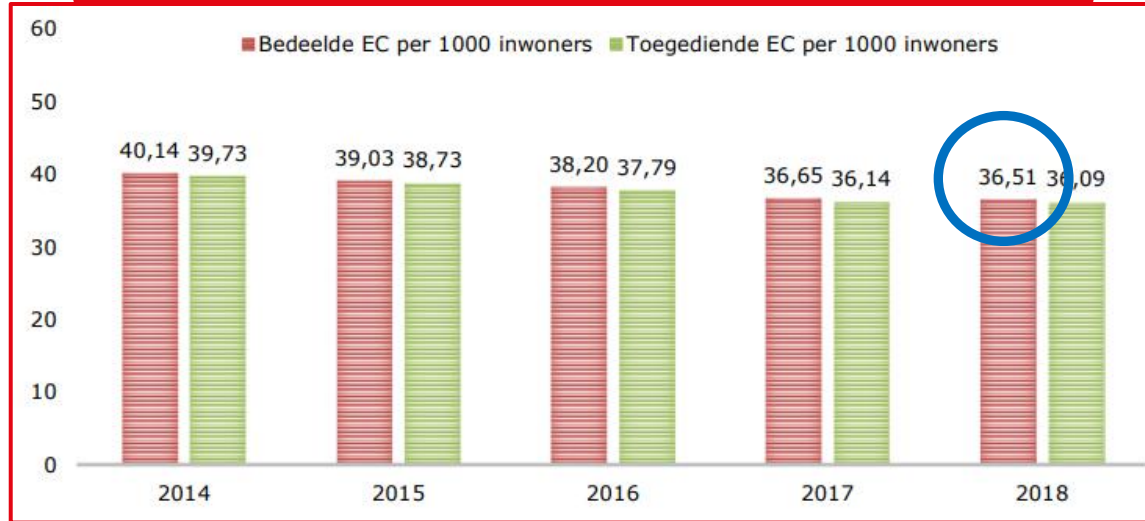
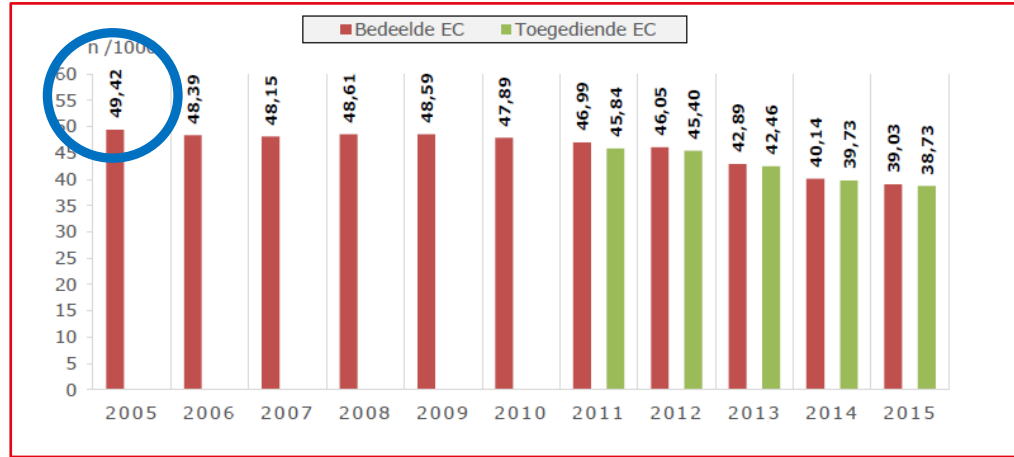
Improvement of transfusion practice and reduction in red blood cell utilization in Belgian hospitals: Results of a national survey and benchmarking

Jana Vanden Broeck^{1,2}  | Katrien Beeckman^{3,4,5} | Evelyne Van Gastel⁶ |
Luc De Keersmaecker⁷ | Timothy Devos⁸ | Christiane Gérard⁹ | Lucien Noens¹⁰ |
Dominique Putzeys¹¹ | Karin Van Poucke¹² | Margareta Haelterman² |
Véronique Deneys¹³ | Rik Schots¹



www.bequint.be

Impact of PBM – evolution number ECL transfused in Belgium



Bron: FAGG jaarverslag Hemovigilantie - 2018

**Thank you for your
attention !**



timothy.devos@uzleuven.be